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=> d his

     (FILE 'HOME' ENTERED AT 13:39:34 ON 30 JAN 2004)

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 13:39:56 ON 30 JAN 2004
L1           384 S REUE K?/AU OR PETERFY M?/AU
L2            14 S L1 AND (LPIN OR LIPIN)
L3             8 DUP REM L2 (6 DUPLICATES REMOVED)
L4          1086 S (LIPIN OR LPIN)
L5             9 S L4 AND (GENE EXPRESSION)
L6             7 DUP REM L5 (2 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 13:45:52 ON 30 JAN 2004

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 13:47:49 ON 30 JAN 2004
L7            16 S L4 AND ADIPOSE
L8            10 DUP REM L7 (6 DUPLICATES REMOVED)
L9             9 S L4 AND MRNA
L10            4 DUP REM L9 (5 DUPLICATES REMOVED)
L11           17 S L4 AND SCREEN?
L12           16 DUP REM L11 (1 DUPLICATE REMOVED)
L13         1045 DUP REM L4 (41 DUPLICATES REMOVED)
L14           15 S L13 AND (NUCLEIC ACID OR PROBE OR GENE PRODUCT)
L15           15 DUP REM L14 (0 DUPLICATES REMOVED)
L16           83 S FATTY LIVER DYSTROPHY
L17           38 DUP REM L16 (45 DUPLICATES REMOVED)
L18            5 S L17 AND (MRNA OR NUCLEIC ACID OR PROBE OR GENE PRODUCT)

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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 09   CA/CAplus records now contain indexing from 1907 to the
                   present
 NEWS  4  DEC 08   INPADOC: Legal Status data reloaded
 NEWS  5  SEP 29   DISSABS now available on STN
 NEWS  6  OCT 10   PCTFULL: Two new display fields added
 NEWS  7  OCT 21   BIOSIS file reloaded and enhanced
 NEWS  8  OCT 28   BIOSIS file segment of TOXCENTER reloaded and enhanced
 NEWS  9  NOV 24   MSDS-CCOHS file reloaded
 NEWS 10  DEC 08   CABA reloaded with left truncation
 NEWS 11  DEC 08   IMS file names changed
 NEWS 12  DEC 09   Experimental property data collected by CAS now available
                   in REGISTRY
 NEWS 13  DEC 09   STN Entry Date available for display in REGISTRY and CA/CAplus
 NEWS 14  DEC 17   DGENE: Two new display fields added
 NEWS 15  DEC 18   BIOTECHNO no longer updated
 NEWS 16  DEC 19   CROPU no longer updated; subscriber discount no longer
                   available
 NEWS 17  DEC 22   Additional INPI reactions and pre-1907 documents added to CAS
                   databases
 NEWS 18  DEC 22   IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
 NEWS 19  DEC 22   ABI-INFORM now available on STN
 NEWS 20  JAN 27   Source of Registration (SR) information in REGISTRY updated
                   and searchable
 NEWS 21  JAN 27   A new search aid, the Company Name Thesaurus, available in
                   CA/CAplus

 NEWS EXPRESS  DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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=> file .biotech caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILES 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
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7 FILES IN THE FILE LIST

=> s reue K?/au or peterfy M?/au
L1 384 REUE K?/AU OR PETERFY M?/AU

=> s l1 and (Lpin or LIPIN)
L2 14 L1 AND (LPIN OR LIPIN)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 8 DUP REM L2 (6 DUPLICATES REMOVED)

=> d ibib abs l3 1-8

L3 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
ACCESSION NUMBER: 2003:460090 BIOSIS
DOCUMENT NUMBER: PREV200300460090
TITLE: Contribution of hepatic futile cycling to glucose intolerance in the **lipin** defective fld mouse.
AUTHOR(S): Xu, Jun [Reprint Author]; Lee, W. N. Paul; Saad, Mohammed; **Reue, Karen**; Kurland, Irwin
CORPORATE SOURCE: Los Angeles, CA, USA
SOURCE: Diabetes, (2003) Vol. 52, No. Supplement 1, pp. A303-A304. print.
Meeting Info.: 63rd Scientific Sessions of the American Diabetes Association. New Orleans, LA, USA. June 13-17, 2003. American Diabetes Association.
ISSN: 0012-1797 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Oct 2003
Last Updated on STN: 8 Oct 2003

L3 ANSWER 2 OF 8 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:698474 SCISEARCH
THE GENUINE ARTICLE: 638KF
TITLE: **Lipin** deficiency attenuates obesity and exacerbates diabetes in leptin deficient ob/ob mice.
AUTHOR: Phan I (Reprint); **Peterfy M**; **Reue K**
CORPORATE SOURCE: Univ Calif Los Angeles, Dept Human Genet, Los Angeles, CA USA; Vet Affairs Greater Los Angeles Healthcare Syst, Los Angeles, CA USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF INVESTIGATIVE MEDICINE, (FEB 2003) Vol. 51, Supp. [1], pp. S147-S147. MA 320.
Publisher: B C DECKER INC, 20 HUGHSON ST SOUTH, PO BOX 620, L C D 1, HAMILTON, ONTARIO L8N 3K7, CANADA.
ISSN: 1081-5589.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L3 ANSWER 3 OF 8 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:698238 SCISEARCH
THE GENUINE ARTICLE: 638KF
TITLE: **Lipin** deficiency attenuates obesity and exacerbates diabetes in leptin deficient ob/ob mice
AUTHOR: Phan J (Reprint); **Peterfy M**; **Reue K**
CORPORATE SOURCE: Univ Calif Los Angeles, Dept Human Genet, Los Angeles, CA USA; Vet Affairs Greater Los Angeles Healthcare Syst, Los Angeles, CA USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF INVESTIGATIVE MEDICINE, (FEB 2003) Vol. 51, Supp. [1], pp. S106-S106. MA 84.
Publisher: B C DECKER INC, 20 HUGHSON ST SOUTH, PO BOX 620, L C D 1, HAMILTON, ONTARIO L8N 3K7, CANADA.
ISSN: 1081-5589.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L3 ANSWER 4 OF 8 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:923224 SCISEARCH
THE GENUINE ARTICLE: 724YZ
TITLE: The role of **lipin** in adipose function and development
AUTHOR: Phan J (Reprint); **Peterfy M**; **Reue K**
SOURCE: OBESITY RESEARCH, (SEP 2003) Vol. 11, Supp. [S], pp. A30-A30.
Publisher: NORTH AMER ASSOC STUDY OBESITY, 8630 FENTON ST, SUITE 918, SILVER SPRING, MD 20910 USA.
ISSN: 1071-7323.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L3 ANSWER 5 OF 8 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-01876 BIOTECHDS
TITLE: New mouse Lpin1 and human LPIN1 genes associated with adiposity/insulin response regulation, useful for screening agents that alter adipose tissue development, or for diagnosing a predilection to lipodystrophy, obesity or diabetes;
vector-mediated recombinant protein gene transfer and expression in host cell for use in diagnosis and therapy
AUTHOR: **REUE K**; **PETERFY M**
PATENT ASSIGNEE: UNIV CALIFORNIA
PATENT INFO: WO 2002059248 1 Aug 2002
APPLICATION INFO: WO 2001-US50237 20 Dec 2001
PRIORITY INFO: US 2000-257772 22 Dec 2000; US 2000-257772 22 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-599767 [64]
AN 2003-01876 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A isolated nucleic acid encoding a polypeptide consisting of human **lipin** 1A, mouse **lipin** 1A or mouse **lipin** 1B, having the mouse Lpin1 or human LPIN1 nucleic acid sequences, or hybridizing to them under stringent conditions, and encoding a **lipin** polypeptide, is new.
DETAILED DESCRIPTION - An isolated nucleic acid encoding the human **lipin** 1A, mouse **lipin** 1A or mouse **lipin** 1B polypeptides, which comprises a 890, 891 or 924 residue amino acid sequence, respectively, given in the specification. The mouse Lpin1 nucleic acid comprises a 5175 base pair sequence, given in the

specification. The human LPIN1 nucleic acid comprises a 5248 base pair sequence, given in the specification. The primers comprise the following sequences: Primer 1: 5'-CAGACAATGAATTACGTGGGGCAGCT-3' Primer 2: 5'-GCTGAGGCTGAATGCATGTCCTGGT-3' Primer 3: 5'-CCATGAATTACGTGGGGCAG-3' Primer 4: 5'-CGCTGAGGCAGAATGAATGTC-3'. INDEPENDENT CLAIMS are also included for the following: (1) (pre)screening an agent that alters adipose tissue development; (2) a polypeptide encoded by the nucleic acid, or an isolated **lipin** polypeptide comprising a polypeptide that comprises an NLIP domain and a CLIP domain; (3) a transgenic animal comprising a recombinantly modified Lpin1/LPIN1 gene, so that the recombinantly modified gene does not transcribe a functional **lipin** protein; (4) identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis; (5) mitigating a symptom of lipodystrophy, obesity, diabetes, atherosclerosis, or related pathology; and (6) inhibiting fat accumulation in a mammal by inhibiting **lipin** expression or activity.

BIOTECHNOLOGY - Preferred Nucleic Acid: The nucleic acid is at least 15 nucleotides in length. The **lipin** polypeptide encoded by the new nucleic acid has a NLIP domain that comprises the consensus sequence of 86 or 159 amino acids defined in the specification. Preferred Antibody: The antibody is a single-chain antibody or a polyclonal antibody. Preferred Animal: The transgenic animal is homozygous for the recombinantly modified Lpin1/LPIN1 gene. The animal is a murine or a mouse. This transgenic animal is chimeric for cells comprising the recombinantly modified Lpin1/LPIN1 gene. Preferred Method: In method (1), screening for an agent that alters adipose tissue development comprises: (a) contacting a cell comprising a Lpin1 gene with a test agent; and (b) detecting a change in the expression or activity of the Lpin1 gene product as compared to the expression or activity of a Lpin1 gene product in a cell that is contacted with the test agent at a lower concentration. A difference in the expression or activity of **lipin** in the contacted cell and control cell with the lower concentration indicates that the agent alters adipose tissue development. The lower concentration is the absence of the test agent. The cell is cultured ex vivo, and the test agent is contacted to an animal comprising a cell containing the Lpin1 gene nucleic acid or **lipin** protein. Prescreening for an agent that alters adipose tissue development comprises: (a) contacting a Lpin1 nucleic acid or a **lipin** protein with a test agent; and (b) detecting specific binding of the test agent to the **lipin** protein or nucleic acid. The method further comprises recording test agents that specifically bind to the Lpin1 nucleic acid or protein in a database of candidate agents that alter adipose tissue development. Preferably, the test agent is not an antibody, not a protein, and not a nucleic acid. The test agent is preferably a small organic molecule. The detecting comprises detecting specific binding of the test agent to the Lpin1 nucleic acid. Detecting specific binding of the test agent to the **lipin** protein is preferably via capillary electrophoresis, a Western blot, mass spectroscopy, enzyme linked immunosorbent assay (ELISA), immunochromatography, or immunohistochemistry. The test agent is contacted directly to the Lpin1 nucleic acid or to the **lipin** protein. The test agent may also be contacted to a cell or to an animal comprising a cell containing the Lpin1 nucleic acid or the **lipin** protein, where the cell is cultured ex vivo. In method (4), identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis comprises: (a) obtaining a biological sample from the organism; and (b) detecting a LPIN1 gene product, where a difference in the amount or activity of the LPIN1 gene product from the organism as compared to a gene product from a normal healthy organism indicates that the organism has or is susceptible to a lipodystrophic phenotype, obesity, diabetes, atherosclerosis or related pathology. In the methods above, the amount of Lpin1 or LPIN1 gene product is detected by detecting Lpin1 mRNA in the sample or LPIN1 mRNA in a cell. The level of Lpin1 or LPIN1 mRNA is measured by hybridizing

the mRNA to a probe that specifically hybridizes to a Lpin1 or LPIN1 nucleic acid, or by using a nucleic acid amplification reaction. The amount of Lpin1 or LPIN1 gene product is detected by detecting the level of a **lipin** protein in the biological sample, preferably via a method comprising capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, or immunohistochemistry. The method may also comprise: (a) obtaining a biological sample from the organism; and (b) detecting a mutation in a Lpin1/LPIN1 gene or gene product from the biological sample. The mutation may be an insertion, a deletion, a missense point mutation or a nonsense point mutation. Detecting is by a method comprising Southern blot, DNA amplification, comparative genomic hybridization, immunohistochemistry or cytogenetics. Detection may also involve detecting a mutation in a polypeptide by capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, or immunohistochemistry. In all the methods above, binding is detected or hybridization is according to method selected from Northern blot, southern blot using DNA derived from the Lpin1 RNA, an array hybridization, an affinity chromatography, and an in situ hybridization. In method (5), mitigating a symptom of lipodystrophy, obesity, diabetes, atherosclerosis, or related pathology comprises modulating the concentration and/or activity of a LPIN1 gene product in a cell of an organism, particularly by upregulating or repressing expression of heterologous or endogenous LPIN1 nucleic acid. Modulation involves transfecting the cell with a vector that expresses a **lipin** protein, where the vector constitutively expresses a **lipin** protein. The expression of the **lipin** protein by the vector is either inducible or constitutive. Preferably, the cell is an adipocyte. In method (6), inhibiting fat accumulation in a mammal comprises: (a) contacting a **lipin** nucleic acid with a ribozyme that specifically cleaves the **lipin** nucleic acid; (b) contacting a **lipin** nucleic acid with a catalytic DNA that specifically cleaves the **lipin** nucleic acid; (c) transfecting a cell comprising a **lipin** gene with a nucleic acid that inactivates the **lipin** gene by homologous recombination with the **lipin** gene; (d) transfecting a cell with a nucleic acid encoding an intrabody that specifically binds a **lipin** polypeptide; or (e) transfecting the cell with a **lipin** antisense molecule. Preferred Probe: The probe is a member of several probes that form an array of probes.

ACTIVITY - Antilipemic; Anorectic; Antidiabetic; Antiarteriosclerotic. No biological data is given.

MECHANISM OF ACTION - Lipin1 Modulator; LIPIN1 Modulator; **Lipin** Inhibitor.

USE - The nucleic acid molecules useful for screening agents that alter adipose tissue development, or for diagnosing or identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis (claimed). The agents obtained are useful for inhibiting fat accumulation in a mammal, or for regulating adiposity and insulin response.

ADMINISTRATION - Dosage is 1-10000, preferably 10-100 micro-g. Administration of **lipin** inhibitors is parenteral, intravenous, topical, oral or local.

EXAMPLE - Northern blot analysis of total RNA from wild type mouse tissue revealed that **lipin** mRNA was expressed in adipose tissue, skeletal muscle and testis. Results showed that Lpin1 encoded a gene product of 891 amino acids. Database searches identified several mouse and human expressed sequence tag (EST)s and genomic sequences with significant similarities to Lpin1. It was also found that the human ortholog of the Lpin1, LPIN1, comprised 5248 base pairs. (87 pages)

L3 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:234245 BIOSIS
DOCUMENT NUMBER: PREV200200234245
TITLE: The role of **lipin** in adipogenesis.

AUTHOR(S): Phan, J. [Reprint author]; **Peterfy, M.**; **Reue, K.**
CORPORATE SOURCE: Department of Medicine, University of California, Los Angeles, Los Angeles, CA, USA
SOURCE: Journal of Investigative Medicine, (January, 2002) Vol. 50, No. 1, pp. 25A. print.
Meeting Info.: Meeting of the American Federation for Medical Research, Western Region. Carmel, California, USA. February 06-09, 2002. American Federation for Medical Research, Western Region.
ISSN: 1081-5589.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Apr 2002
Last Updated on STN: 10 Apr 2002

L3 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:234138 BIOSIS
DOCUMENT NUMBER: PREV200200234138
TITLE: The role of **lipin** in adipogenesis.
AUTHOR(S): Phan, J. [Reprint author]; **Peterfy, M.**; **Reue, K.**
CORPORATE SOURCE: Department of Medicine, University of California, Los Angeles, CA, USA
SOURCE: Journal of Investigative Medicine, (January, 2002) Vol. 50, No. 1, pp. 3A. print.
Meeting Info.: Meeting of the American Federation for Medical Research, Western Region. Carmel, California, USA. February 06-09, 2002. American Federation for Medical Research, Western Region.
ISSN: 1081-5589.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Apr 2002
Last Updated on STN: 10 Apr 2002

L3 ANSWER 8 OF 8 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001099615 MEDLINE
DOCUMENT NUMBER: 20578762 PubMed ID: 11138012
TITLE: Lipodystrophy in the fld mouse results from mutation of a new gene encoding a nuclear protein, **lipin**.
AUTHOR: **Peterfy M**; Phan J; Xu P; **Reue K**
CORPORATE SOURCE: Department of Medicine, University of California, Los Angeles, California, USA.
CONTRACT NUMBER: HL24841 (NHLBI)
SOURCE: NATURE GENETICS, (2001 Jan) 27 (1) 121-4.
Journal code: 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF180471; GENBANK-AF286724; GENBANK-AL132654; GENBANK-P32567; GENBANK-Q14693; GENBANK-Q92539
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB Mice carrying mutations in the fatty liver dystrophy (fld) gene have features of human lipodystrophy, a genetically heterogeneous group of disorders characterized by loss of body fat, fatty liver,

hypertriglyceridemia and insulin resistance. Through positional cloning, we have isolated the gene responsible and characterized two independent mutant alleles, fld and fld(2J). The gene (Lpin1) encodes a novel nuclear protein which we have named **lipin**. Consistent with the observed reduction of adipose tissue mass in fld and fld(2J)mice, wild-type Lpin1 mRNA is expressed at high levels in adipose tissue and is induced during differentiation of 3T3-L1 pre-adipocytes. Our results indicate that **lipin** is required for normal adipose tissue development, and provide a candidate gene for human lipodystrophy. **Lipin** defines a novel family of nuclear proteins containing at least three members in mammalian species, and homologs in distantly related organisms from human to yeast.

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=> d his

     (FILE 'HOME' ENTERED AT 13:39:34 ON 30 JAN 2004)

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 13:39:56 ON 30 JAN 2004
L1           384 S REUE K?/AU OR PETERFY M?/AU
L2            14 S L1 AND (LPIN OR LIPIN)
L3             8 DUP REM L2 (6 DUPLICATES REMOVED)

=> s (LIPIN or LPIN)
L4         1086 (LIPIN OR LPIN)

=> s l4 and (gene expression)
L5            9 L4 AND (GENE EXPRESSION)

=>

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6             7 DUP REM L5 (2 DUPLICATES REMOVED)

=> d ibib abs l6 1-7

L6   ANSWER 1 OF 7     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2004021978      IN-PROCESS
DOCUMENT NUMBER:     PubMed ID: 14718385
TITLE:               Multiple types of skeletal muscle atrophy involve a common
                     program of changes in gene expression.
AUTHOR:              Lecker Stewart H; Jagoe R Thomas; Gilbert Alexander; Gomes
                     Marcelo; Baracos Vickie; Bailey James; Price S Russ; Mitch
                     William E; Goldberg Alfred L
CORPORATE SOURCE:    Renal Unit, Beth Israel Deaconess Medical Center, Boston,
                     Massachusetts, USA.
CONTRACT NUMBER:     DK02727 (NIDDK)
     DK37175 (NIDDK)
     DK50740 (NIDDK)
     DK63658 (NIDDK)
SOURCE:              FASEB journal : official publication of the Federation of
                     American Societies for Experimental Biology, (2004 Jan) 18
                     (1) 39-51.
                     Journal code: 8804484. ISSN: 1530-6860.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:          Entered STN: 20040115
                     Last Updated on STN: 20040115
AB   Skeletal muscle atrophy is a debilitating response to starvation and many
     systemic diseases including diabetes, cancer, and renal failure.  We had
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proposed that a common set of transcriptional adaptations underlie the loss of muscle mass in these different states. To test this hypothesis, we used cDNA microarrays to compare the changes in content of specific mRNAs in muscles atrophying from different causes. We compared muscles from fasted mice, from rats with cancer cachexia, streptozotocin-induced diabetes mellitus, uremia induced by subtotal nephrectomy, and from pair-fed control rats. Although the content of >90% of mRNAs did not change, including those for the myofibrillar apparatus, we found a common set of genes (termed atrogins) that were induced or suppressed in muscles in these four catabolic states. Among the strongly induced genes were many involved in protein degradation, including polyubiquitins, Ub fusion proteins, the Ub ligases atrogin-1/MAFbx and MuRF-1, multiple but not all subunits of the 20S proteasome and its 19S regulator, and cathepsin L. Many genes required for ATP production and late steps in glycolysis were down-regulated, as were many transcripts for extracellular matrix proteins. Some genes not previously implicated in muscle atrophy were dramatically up-regulated (**lipin**, metallothionein, AMP deaminase, RNA helicase-related protein, TG interacting factor) and several growth-related mRNAs were down-regulated (P311, JUN, IGF-1-BP5). Thus, different types of muscle atrophy share a common transcriptional program that is activated in many systemic diseases.

L6 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003460683 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14522948
TITLE: Local regulation of fat metabolism in peripheral nerves.
AUTHOR: Verheijen Mark H G; Chrast Roman; Burrola Patrick; Lemke Greg
CORPORATE SOURCE: Molecular Neurobiology Laboratory, The Salk Institute, La Jolla, California 92037, USA.
SOURCE: Genes & development, (2003 Oct 1) 17 (19) 2450-64. Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20031003
Last Updated on STN: 20031218
Entered Medline: 20031117

AB We comprehensively analyzed **gene expression** during peripheral nerve development by performing microarray analyses of premyelinating, myelinating, and postmyelinating mouse sciatic nerves, and we generated a database of candidate genes to be tested in mapped peripheral neuropathies. Unexpectedly, we identified a large cluster of genes that are (1) maximally expressed only in the mature nerve, after myelination is complete, and (2) tied to the metabolism of storage (energy) lipids. Many of these late-onset genes are expressed by adipocytes, which we find constitute the bulk of the epineurial compartment of the adult nerve. However, several such genes, including SREBP-1, SREBP-2, and Lpin1, are also expressed in the endoneurium. We find that Lpin1 null mutations lead to lipoatrophy of the epineurium, and to the dysregulation of a battery of genes required for the regulation of storage lipid metabolism in both the endoneurium and peri/epineurium. Together with the observation that these mutations also result in peripheral neuropathy, our findings demonstrate a crucial role for local storage lipid metabolism in mature peripheral nerve function, and have important implications for the understanding and treatment of peripheral neuropathies that are commonly associated with metabolic diseases such as lipodystrophy and diabetes.

L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:212043 CAPLUS
DOCUMENT NUMBER: 138:383344

TITLE: **Gene expression** profiles of nondiabetic and diabetic obese mice suggest a role of hepatic lipogenic capacity in diabetes susceptibility
AUTHOR(S): Lan, Hong; Rabaglia, Mary E.; Stoehr, Jonathan P.; Nadler, Samuel T.; Schueler, Kathryn L.; Zou, Fei; Yandell, Brian S.; Attie, Alan D.
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Diabetes (2003), 52(3), 688-700
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Obesity is a strong risk factor for the development of type 2 diabetes. The authors have previously reported that in adipose tissue of obese (ob/ob) mice, the expression of adipogenic genes is decreased. When made genetically obese, the BTBR mouse strain is diabetes susceptible and the C57BL/6J (B6) strain is diabetes resistant. The authors used DNA microarrays and RT-PCR to compare the **gene expression** in BTBR-ob/ob vs. B6-ob/ob mice in adipose tissue, liver, skeletal muscle, and pancreatic islets. The authors' results show: (1) there is an increased expression of genes involved in inflammation in adipose tissue of diabetic mice; (2) lipogenic **gene expression** was lower in adipose tissue of diabetes-susceptible mice, and it continued to decrease with the development of diabetes, compared with diabetes-resistant obese mice; (3) hepatic expression of lipogenic enzymes was increased and the hepatic triglyceride content was greatly elevated in diabetes-resistant obese mice; (4) hepatic expression of gluconeogenic genes was suppressed at the prediabetic stage but not at the onset of diabetes; and (5) genes normally not expressed in skeletal muscle and pancreatic islets were expressed in these tissues in the diabetic mice. The authors propose that increased hepatic lipogenic capacity protects the B6-ob/ob mice from the development of type 2 diabetes.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2002619215 MEDLINE
DOCUMENT NUMBER: 22263608 PubMed ID: 12376568
TITLE: An evolutionarily conserved fission yeast protein, Ned1, implicated in normal nuclear morphology and chromosome stability, interacts with Dis3, Pim1/RCC1 and an essential nucleoporin.
AUTHOR: Tange Yoshie; Hirata Aiko; Niwa Osami
CORPORATE SOURCE: Kazusa DNA Research Institute, 2-6-7 Kazusa-kamatari, Kisarazu, Chiba 292-0818, Japan.
SOURCE: JOURNAL OF CELL SCIENCE, (2002 Nov 15) 115 (Pt 22) 4375-85. Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20021012
Last Updated on STN: 20030703
Entered Medline: 20030702

AB We identified a novel fission yeast gene, ned1(+), with pleiotropic mutations that have a high incidence of chromosome missegregation, aberrantly shaped nuclei, overdeveloped endoplasmic reticulum-like membranes, and increased sensitivity to a microtubule destabilizing agent. Ned1 protein, which was phosphorylated in a growth-related manner, interacted in a yeast two-hybrid system with Dis3 as well as with Pim1/RCC1 (nucleotide exchange factor for Ran). Ned1 also interacted with an essential nucleoporin, a probable homologue of mammalian Nup98/96. The

ned1 gene displayed a variety of genetic interactions with factors involved in nuclear transport and chromosome segregation, including the crm1 (exportin), spi1 (small GTPase Ran), pim1, and dis genes. A substitution mutation that affected the two-hybrid interaction with Dis3 increased chromosome instability, suggesting the functional importance of the interaction. Overproduction of Ned1 protein induced formation of an abnormal microtubule bundle within the nucleus, apparently independently of the spindle pole body, but dependent on pim1(+) activity. The ned1(+) gene belongs to an evolutionarily conserved gene family, which includes the mouse **Lpin** genes, one of whose mutations is responsible for lipodystrophy.

L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:713426 CAPLUS
DOCUMENT NUMBER: 138:51181
TITLE: Paraquat-induced **gene expression** in rat lung tissues using a differential display reverse transcription-polymerase chain reaction
AUTHOR(S): Tomita, Masafumi; Nohno, Tsutomu; Okuyama, Toshiko; Nishimatsu, Shin-ichiro; Adachi, Junko
CORPORATE SOURCE: Department of Legal Medicine, Kawasaki Medical School, Kurashiki, 701-0192, Japan
SOURCE: Archives of Toxicology (2002), 76(9), 530-537
CODEN: ARTODN; ISSN: 0340-5761
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Increased formation of reactive oxygen species is a cause of paraquat (PQ)-induced injury and also provides a link between the signaling pathways and transcriptional events that regulate the expression of a large no. of genes. However, the mol. mechanisms involved in PQ-induced injury remain unclear. To investigate the changes in **gene expression** at the onset of PQ injury, the authors used the differential display-polymerase chain reaction (PCR) method. Rats were treated i.p. with 20 mg/kg PQ, and after 3 h the lungs were immediately excised. Samples of mRNA from normal and treated rats were used to prep. radiolabeled cDNAs, which were electrophoresed. Then the transcription levels were compared. The authors isolated 26 fragments of cDNA that were potentially affected by PQ, and detd. their nucleotide sequences. Six clones of interest were selected and analyzed further. The reverse transcript-PCR based on their sequence information confirmed the differential expression for five clones: four clones were up-regulated and one was down-regulated. The authors were particularly interested in two genes that had homol. with the known gene: TATA box-binding protein-assocd. factor, RNA polymerase II, B, 150 kDa (TAFIIB), and a candidate gene for lipodystrophy, Lpin2. Both genes were significantly up-regulated within 3 h of PQ intake and the stimulation continued during our 24-h observation period. In addn., up-regulation of Lpin2 was obsd. in the lungs, but not in the liver and kidneys. In situ hybridization using lung sections showed that the expression of both genes was strongly visualized in Clara cells and in alveolar macrophages. These findings suggest a stimulation of transcription levels and changes in lipid metab. in Clara cells and in macrophages in the lungs, which result in their playing a crucial role at the onset of PQ-driven pulmonary injury.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2001099615 MEDLINE
DOCUMENT NUMBER: 20578762 PubMed ID: 11138012
TITLE: Lipodystrophy in the fld mouse results from mutation of a new gene encoding a nuclear protein, **lipin**.
AUTHOR: Peterfy M; Phan J; Xu P; Reue K
CORPORATE SOURCE: Department of Medicine, University of California, Los

Angeles, California, USA.
CONTRACT NUMBER: HL24841 (NHLBI)
SOURCE: NATURE GENETICS, (2001 Jan) 27 (1) 121-4.
Journal code: 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF180471; GENBANK-AF286724; GENBANK-AL132654; GENBANK-P32567; GENBANK-Q14693; GENBANK-Q92539
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB Mice carrying mutations in the fatty liver dystrophy (fld) gene have features of human lipodystrophy, a genetically heterogeneous group of disorders characterized by loss of body fat, fatty liver, hypertriglyceridemia and insulin resistance. Through positional cloning, we have isolated the gene responsible and characterized two independent mutant alleles, fld and fld(2J). The gene (Lpin1) encodes a novel nuclear protein which we have named **lipin**. Consistent with the observed reduction of adipose tissue mass in fld and fld(2J)mice, wild-type Lpin1 mRNA is expressed at high levels in adipose tissue and is induced during differentiation of 3T3-L1 pre-adipocytes. Our results indicate that **lipin** is required for normal adipose tissue development, and provide a candidate gene for human lipodystrophy. **Lipin** defines a novel family of nuclear proteins containing at least three members in mammalian species, and homologs in distantly related organisms from human to yeast.

L6 ANSWER 7 OF 7 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 93:425515 SCISEARCH
THE GENUINE ARTICLE: LL310
TITLE: IS AN ACTIVATOR PROTEIN-2-LIKE TRANSCRIPTION FACTOR INVOLVED IN REGULATING **GENE-EXPRESSION** DURING NITROGEN LIMITATION IN FUNGI
AUTHOR: DHAWALE S S (Reprint)
CORPORATE SOURCE: INDIANA UNIV PURDUE UNIV, FT WAYNE, IN, 46805 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (JUL 1993) Vol. 59, No. 7, pp. 2335-2338.
ISSN: 0099-2240.
DOCUMENT TYPE: Note; Journal
FILE SEGMENT: LIFE; AGRI
LANGUAGE: ENGLISH
REFERENCE COUNT: 25
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The upstream sequences of all published **lipin** peroxidase and manganese peroxidase genomic clones from Phanerochaete chrysosporium were analyzed. This analysis revealed the presence of putative activator protein-2 (AP-2) recognition sequences in 11 of 15 lignin peroxidase genes. The lignin peroxidase clone GLG6 and the manganese peroxidase gene (mnp-1) have two copies of putative AP-2 sequence in the upstream region. Interestingly, the lignin peroxidase gene VLG4 of another white rot fungus, Trametes versicolor, and the nit-2 gene of Neurospora crassa also contain putative AP-2-binding sequences. Since all of these genes are regulated by nutrient nitrogen, I hypothesize that an AP-2-like transcription factor may be involved in inducing **gene expression** during nitrogen limitation in fungi.

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     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 13:39:56 ON 30 JAN 2004
L1           384 S REUE K?/AU OR PETERFY M?/AU
L2            14 S L1 AND (LPIN OR LIPIN)
L3             8 DUP REM L2 (6 DUPLICATES REMOVED)
L4          1086 S (LIPIN OR LPIN)
L5             9 S L4 AND (GENE EXPRESSION)
L6             7 DUP REM L5 (2 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 13:45:52 ON 30 JAN 2004

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 13:47:49 ON 30 JAN 2004

=> s l4 and adipose
L7            16 L4 AND ADIPOSE

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8            10 DUP REM L7 (6 DUPLICATES REMOVED)

=> d ibib abs l8 1-10

L8   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:212043  CAPLUS
DOCUMENT NUMBER:          138:383344
TITLE:                    Gene expression profiles of nondiabetic and diabetic
                          obese mice suggest a role of hepatic lipogenic
                          capacity in diabetes susceptibility
AUTHOR(S):                Lan, Hong; Rabaglia, Mary E.; Stoehr, Jonathan P.;
                          Nadler, Samuel T.; Schueler, Kathryn L.; Zou, Fei;
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Yandell, Brian S.; Attie, Alan D.
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Diabetes (2003), 52(3), 688-700
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Obesity is a strong risk factor for the development of type 2 diabetes. The authors have previously reported that in **adipose** tissue of obese (ob/ob) mice, the expression of adipogenic genes is decreased. When made genetically obese, the BTBR mouse strain is diabetes susceptible and the C57BL/6J (B6) strain is diabetes resistant. The authors used DNA microarrays and RT-PCR to compare the gene expression in BTBR-ob/ob vs. B6-ob/ob mice in **adipose** tissue, liver, skeletal muscle, and pancreatic islets. The authors' results show: (1) there is an increased expression of genes involved in inflammation in **adipose** tissue of diabetic mice; (2) lipogenic gene expression was lower in **adipose** tissue of diabetes-susceptible mice, and it continued to decrease with the development of diabetes, compared with diabetes-resistant obese mice; (3) hepatic expression of lipogenic enzymes was increased and the hepatic triglyceride content was greatly elevated in diabetes-resistant obese mice; (4) hepatic expression of gluconeogenic genes was suppressed at the prediabetic stage but not at the onset of diabetes; and (5) genes normally not expressed in skeletal muscle and pancreatic islets were expressed in these tissues in the diabetic mice. The authors propose that increased hepatic lipogenic capacity protects the B6-ob/ob mice from the development of type 2 diabetes.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:923224 SCISEARCH
THE GENUINE ARTICLE: 724YZ
TITLE: The role of **lipin** in **adipose** function and development
AUTHOR: Phan J (Reprint); Peterfy M; Reue K
SOURCE: OBESITY RESEARCH, (SEP 2003) Vol. 11, Supp. [S], pp. A30-A30.
Publisher: NORTH AMER ASSOC STUDY OBESITY, 8630 FENTON ST, SUITE 918, SILVER SPRING, MD 20910 USA.
ISSN: 1071-7323.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L8 ANSWER 3 OF 10 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-01876 BIOTECHDS
TITLE: New mouse Lpin1 and human LPIN1 genes associated with adiposity/insulin response regulation, useful for screening agents that alter **adipose** tissue development, or for diagnosing a predilection to lipodystrophy, obesity or diabetes;
vector-mediated recombinant protein gene transfer and expression in host cell for use in diagnosis and therapy
AUTHOR: REUE K; PETERFY M
PATENT ASSIGNEE: UNIV CALIFORNIA
PATENT INFO: WO 2002059248 1 Aug 2002
APPLICATION INFO: WO 2001-US50237 20 Dec 2001
PRIORITY INFO: US 2000-257772 22 Dec 2000; US 2000-257772 22 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-599767 [64]
AN 2003-01876 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - A isolated nucleic acid encoding a polypeptide consisting of human **lipin** 1A, mouse **lipin** 1A or mouse **lipin** 1B, having the mouse Lpin1 or human LPIN1 nucleic acid sequences, or hybridizing to them under stringent conditions, and encoding a **lipin** polypeptide, is new.

DETAILED DESCRIPTION - An isolated nucleic acid encoding the human **lipin** 1A, mouse **lipin** 1A or mouse **lipin** 1B polypeptides, which comprises a 890, 891 or 924 residue amino acid sequence, respectively, given in the specification. The mouse Lpin1 nucleic acid comprises a 5175 base pair sequence, given in the specification. The human LPIN1 nucleic acid comprises a 5248 base pair sequence, given in the specification. The primers comprise the following sequences: Primer 1: 5'-CAGACAATGAATTACGTGGGGCAGCT-3' Primer 2: 5'-GCTGAGGCTGAATGCATGTCCTGGT-3' Primer 3: 5'-CCATGAATTACGTGGGGCAG-3' Primer 4: 5'-CGCTGAGGCAGAATGAATGTC-3'. INDEPENDENT CLAIMS are also included for the following: (1) (pre)screening an agent that alters **adipose** tissue development; (2) a polypeptide encoded by the nucleic acid, or an isolated **lipin** polypeptide comprising a polypeptide that comprises an NLIP domain and a CLIP domain; (3) a transgenic animal comprising a recombinantly modified Lpin1/LPIN1 gene, so that the recombinantly modified gene does not transcribe a functional **lipin** protein; (4) identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis; (5) mitigating a symptom of lipodystrophy, obesity, diabetes, atherosclerosis, or related pathology; and (6) inhibiting fat accumulation in a mammal by inhibiting **lipin** expression or activity.

BIOTECHNOLOGY - Preferred Nucleic Acid: The nucleic acid is at least 15 nucleotides in length. The **lipin** polypeptide encoded by the new nucleic acid has a NLIP domain that comprises the consensus sequence of 86 or 159 amino acids defined in the specification. Preferred Antibody: The antibody is a single-chain antibody or a polyclonal antibody. Preferred Animal: The transgenic animal is homozygous for the recombinantly modified Lpin1/LPIN1 gene. The animal is a murine or a mouse. This transgenic animal is chimeric for cells comprising the recombinantly modified Lpin1/LPIN1 gene. Preferred Method: In method (1), screening for an agent that alters **adipose** tissue development comprises: (a) contacting a cell comprising a Lpin1 gene with a test agent; and (b) detecting a change in the expression or activity of the Lpin1 gene product as compared to the expression or activity of a Lpin1 gene product in a cell that is contacted with the test agent at a lower concentration. A difference in the expression or activity of **lipin** in the contacted cell and control cell with the lower concentration indicates that the agent alters **adipose** tissue development. The lower concentration is the absence of the test agent. The cell is cultured ex vivo, and the test agent is contacted to an animal comprising a cell containing the Lpin1 gene nucleic acid or **lipin** protein. Prescreening for an agent that alters **adipose** tissue development comprises: (a) contacting a Lpin1 nucleic acid or a **lipin** protein with a test agent; and (b) detecting specific binding of the test agent to the **lipin** protein or nucleic acid. The method further comprises recording test agents that specifically bind to the Lpin1 nucleic acid or protein in a database of candidate agents that alter **adipose** tissue development. Preferably, the test agent is not an antibody, not a protein, and not a nucleic acid. The test agent is preferably a small organic molecule. The detecting comprises detecting specific binding of the test agent to the Lpin1 nucleic acid. Detecting specific binding of the test agent to the **lipin** protein is preferably via capillary electrophoresis, a Western blot, mass spectroscopy, enzyme linked immunosorbent assay (ELISA), immunochromatography, or immunohistochemistry. The test agent is contacted directly to the Lpin1 nucleic acid or to the **lipin** protein. The test agent may also

be contacted to a cell or to an animal comprising a cell containing the Lpin1 nucleic acid or the **lipin** protein, where the cell is cultured ex vivo. In method (4), identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis comprises: (a) obtaining a biological sample from the organism; and (b) detecting a LPIN1 gene product, where a difference in the amount or activity of the LPIN1 gene product from the organism as compared to a gene product from a normal healthy organism indicates that the organism has or is susceptible to a lipodystrophic phenotype, obesity, diabetes, atherosclerosis or related pathology. In the methods above, the amount of Lpin1 or LPIN1 gene product is detected by detecting Lpin1 mRNA in the sample or LPIN1 mRNA in a cell. The level of Lpin1 or LPIN1 mRNA is measured by hybridizing the mRNA to a probe that specifically hybridizes to a Lpin1 or LPIN1 nucleic acid, or by using a nucleic acid amplification reaction. The amount of Lpin1 or LPIN1 gene product is detected by detecting the level of a **lipin** protein in the biological sample, preferably via a method comprising capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, or immunohistochemistry. The method may also comprise: (a) obtaining a biological sample from the organism; and (b) detecting a mutation in a Lpin1/LPIN1 gene or gene product from the biological sample. The mutation may be an insertion, a deletion, a missense point mutation or a nonsense point mutation. Detecting is by a method comprising Southern blot, DNA amplification, comparative genomic hybridization, immunohistochemistry or cytogenetics. Detection may also involve detecting a mutation in a polypeptide by capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, or immunohistochemistry. In all the methods above, binding is detected or hybridization is according to method selected from Northern blot, southern blot using DNA derived from the Lpin1 RNA, an array hybridization, an affinity chromatography, and an in situ hybridization. In method (5), mitigating a symptom of lipodystrophy, obesity, diabetes, atherosclerosis, or related pathology comprises modulating the concentration and/or activity of a LPIN1 gene product in a cell of an organism, particularly by upregulating or repressing expression of heterologous or endogenous LPIN1 nucleic acid. Modulation involves transfecting the cell with a vector that expresses a **lipin** protein, where the vector constitutively expresses a **lipin** protein. The expression of the **lipin** protein by the vector is either inducible or constitutive. Preferably, the cell is an adipocyte. In method (6), inhibiting fat accumulation in a mammal comprises: (a) contacting a **lipin** nucleic acid with a ribozyme that specifically cleaves the **lipin** nucleic acid; (b) contacting a **lipin** nucleic acid with a catalytic DNA that specifically cleaves the **lipin** nucleic acid; (c) transfecting a cell comprising a **lipin** gene with a nucleic acid that inactivates the **lipin** gene by homologous recombination with the **lipin** gene; (d) transfecting a cell with a nucleic acid encoding an intrabody that specifically binds a **lipin** polypeptide; or (e) transfecting the cell with a **lipin** antisense molecule.
Preferred Probe: The probe is a member of several probes that form an array of probes.

ACTIVITY - Antilipemic; Anorectic; Antidiabetic; Antiarteriosclerotic. No biological data is given.

MECHANISM OF ACTION - Lipin1 Modulator; LIPIN1 Modulator; **Lipin** Inhibitor.

USE - The nucleic acid molecules useful for screening agents that alter **adipose** tissue development, or for diagnosing or identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis (claimed). The agents obtained are useful for inhibiting fat accumulation in a mammal, or for regulating adiposity and insulin response.

ADMINISTRATION - Dosage is 1-10000, preferably 10-100 micro-g. Administration of **lipin** inhibitors is parenteral, intravenous,

topical, oral or local.

EXAMPLE - Northern blot analysis of total RNA from wild type mouse tissue revealed that **lipin** mRNA was expressed in **adipose** tissue, skeletal muscle and testis. Results showed that Lpin1 encoded a gene product of 891 amino acids. Database searches identified several mouse and human expressed sequence tag (EST)s and genomic sequences with significant similarities to Lpin1. It was also found that the human ortholog of the Lpin1, LPIN1, comprised 5248 base pairs. (87 pages)

L8 ANSWER 4 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 2
ACCESSION NUMBER: 2002:98932 SCISEARCH
THE GENUINE ARTICLE: 514PK
TITLE: Insulin-stimulated phosphorylation of **lipin** mediated by the mammalian target of rapamycin
AUTHOR: Huffman T A; Mothe-Satney I; Lawrence J C (Reprint)
CORPORATE SOURCE: Univ Virginia, Hlth Syst, Dept Pharmacol, Sch Med, POB 800735, 1300 Jefferson Pk Ave, Charlottesville, VA 22908 USA (Reprint); Univ Virginia, Hlth Syst, Dept Pharmacol, Sch Med, Charlottesville, VA 22908 USA; Univ Virginia, Hlth Syst, Dept Med, Sch Med, Charlottesville, VA 22908 USA
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (22 JAN 2002) Vol. 99, No. 2, pp. 1047-1052.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418 USA.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 44

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The phosphorylation of a previously uncharacterized protein of apparent Mr approximate to 140,000 was found to be increased when rat adipocytes were incubated with insulin. The sequences of peptides generated by digesting the protein with trypsin matched perfectly with sequences in mouse **lipin**. **Lipin** is the product of the gene that is mutated in fatty liver dystrophy (fld) mice [Peterfy, M., Phan, J., Xu, P. & Reue, K (2001) Nat. Genet. 27, 121-124], which exhibit several phenotypic abnormalities including hyperlipidemia, defects in adipocyte differentiation, impaired glucose tolerance, and slow growth. When immunoblots were prepared with **lipin** antibodies, both endogenous adipocyte **lipin** and recombinant **lipin** overexpressed in HEK293 cells appeared as bands ranging in apparent Mr from 120,000 to 140,000. Incubating adipocytes with insulin decreased the electrophoretic mobility and stimulated the phosphorylation of both Ser and Thr residues in **lipin**. The effects of insulin were abolished by inhibitors of phosphatidylinositol 3-OH kinase, and by rapamycin, a specific inhibitor of the mammalian target of rapamcyin (mTOR). The inhibition by rapamycin was blocked by FK506, which competitively inhibits those effects of rapamycin that are mediated by inhibition of mTOR. Moreover, amino acids, which activate mTOR, mimicked insulin by increasing **lipin** phosphorylation in a rapamycin-sensitive manner. Thus, **lipin** represents a target of the mTOR pathway, and potentially links this nutrient-sensing pathway to adipocyte development.

L8 ANSWER 5 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:234245 BIOSIS
DOCUMENT NUMBER: PREV200200234245
TITLE: The role of **lipin** in adipogenesis.
AUTHOR(S): Phan, J. [Reprint author]; Peterfy, M.; Reue, K.
CORPORATE SOURCE: Department of Medicine, University of California, Los Angeles, Los Angeles, CA, USA

SOURCE: Journal of Investigative Medicine, (January, 2002) Vol. 50, No. 1, pp. 25A. print.
Meeting Info.: Meeting of the American Federation for Medical Research, Western Region. Carmel, California, USA. February 06-09, 2002. American Federation for Medical Research, Western Region.
ISSN: 1081-5589.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Apr 2002
Last Updated on STN: 10 Apr 2002

L8 ANSWER 6 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:318094 SCISEARCH
THE GENUINE ARTICLE: 420KN
TITLE: Structure-function relationships of hormone-sensitive lipase
AUTHOR: Osterlund T (Reprint)
CORPORATE SOURCE: Karolinska Inst, Novum, Dept Biosci, S-14157 Huddinge, Sweden (Reprint)
COUNTRY OF AUTHOR: Sweden
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (APR 2001) Vol. 268, No. 7, pp. 1899-1907.
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0014-2956.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 79
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Research into the structure-function relationships of lipases and esterases has increased significantly during the past decade. Of particular importance has been the deduction of several crystal structures, providing a new basis for understanding these enzymes. The generated insights have, together with cloning and expression, aided studies on structure-function relationships of hormone-sensitive lipase (HSL). Novel phosphorylation sites have been identified in HSL, which are probably important for activation of HSL and lipolysis. Functional and structural analyses have revealed features in HSL common to lipases and esterases. In particular, the catalytic core with a catalytic triad has been unveiled. Furthermore, the investigations have given clear suggestions with regard to the identity of functional and structural domains of HSL. In the present paper, these studies on HSL structure-function relationships and short-term regulation are reviewed, and the results presented in relation to other discoveries in regulated lipolysis.

L8 ANSWER 7 OF 10 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001099615 MEDLINE
DOCUMENT NUMBER: 20578762 PubMed ID: 11138012
TITLE: Lipodystrophy in the fld mouse results from mutation of a new gene encoding a nuclear protein, **lipin**.
AUTHOR: Peterfy M; Phan J; Xu P; Reue K
CORPORATE SOURCE: Department of Medicine, University of California, Los Angeles, California, USA.
CONTRACT NUMBER: HL24841 (NHLBI)
SOURCE: NATURE GENETICS, (2001 Jan) 27 (1) 121-4.
Journal code: 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-AF180471; GENBANK-AF286724; GENBANK-AL132654; GENBANK-P32567; GENBANK-Q14693; GENBANK-Q92539
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB Mice carrying mutations in the fatty liver dystrophy (fld) gene have features of human lipodystrophy, a genetically heterogeneous group of disorders characterized by loss of body fat, fatty liver, hypertriglyceridemia and insulin resistance. Through positional cloning, we have isolated the gene responsible and characterized two independent mutant alleles, fld and fld(2J). The gene (Lpin1) encodes a novel nuclear protein which we have named **lipin**. Consistent with the observed reduction of **adipose** tissue mass in fld and fld(2J)mice, wild-type Lpin1 mRNA is expressed at high levels in **adipose** tissue and is induced during differentiation of 3T3-L1 pre-adipocytes. Our results indicate that **lipin** is required for normal **adipose** tissue development, and provide a candidate gene for human lipodystrophy. **Lipin** defines a novel family of nuclear proteins containing at least three members in mammalian species, and homologs in distantly related organisms from human to yeast.

L8 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:244556 BIOSIS
DOCUMENT NUMBER: PREV198477077540; BA77:77540
TITLE: ACYL GROUP DISTRIBUTIONS IN TISSUE LIPIDS OF RATS FED EVENING PRIMROSE OIL GAMMA LINOLENIC-ACID PLUS LINOLEIC-ACID OR SOYBEAN OIL ALPHA LINOLENIC-ACID PLUS LINOLEIC-ACID.
AUTHOR(S): HOY C-E [Reprint author]; HOLMER G; KAUR N; BYRJALSEN I; KIRSTEIN D
CORPORATE SOURCE: DEP BIOCHEM NUTRITION, TECHNICAL UNIV DENMARK, BUILD 224, DK-2800 LYNGBY, DENMARK
SOURCE: Lipids, (1983) Vol. 18, No. 11, pp. 760-771.
CODEN: LPDSAP. ISSN: 0024-4201.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Three groups of rats were fed diets with either 10 wt% of evening primrose oil, safflower oil or soybean oil for 11 wk. Diets contained 7.1 wt% linoleic acid + 0.8 wt% .gamma.-linolenic acid, 7.6 wt% linoleic acid, or 5.3 wt% linoleic acid + 0.7 wt% .alpha.-linolenic acid, respectively. In liver mitochondria as well as in heart, dietary .gamma.-linolenic acid did not affect the fatty acid profiles of phosphatidylcholines (PC), phosphatidylethanolamines (PE) or cardiolipins (CL), whereas dietary .alpha.-linolenic acid caused an increased formation of (n-3) polyunsaturated fatty acids (PUFA). The liver .DELTA.6- and .DELTA.5-desaturase activities determined in vitro were not affected by the dietary fats. In brain PE, which are rich in C22- and C20-(n-3) PUFA, as well as in testes PC and PE, which are rich in (n-6) PUFA, no effects were found from a partial replacement of dietary linoleic acid with .gamma.-linolenic acid or .alpha.-linolenic acid. In kidney PC, PE, phosphatidylinositol (PI) and CL, 20:3(n-6) was moderately elevated to .apprx. 1% following intake of .gamma.-linolenic acid, whereas partial replacement of linoleic acid with .alpha.-linolenic acid was followed by increased deposition of 22:6(n-3) in PC and PE of testes and kidney. No general effect of evening primrose oil on the content of (n-6) PUFA in rat tissue phospholipids was observed, whereas a significant incorporation of .gamma.-linolenic acid into liver and **adipose** tissue triglycerides was found.

L8 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1980:256271 BIOSIS
DOCUMENT NUMBER: PREV198070048767; BA70:48767

TITLE: PHOSPHO LIPID SYNTHESIS IN BROWN **ADIPOSE** TISSUE MITOCHONDRIA.
AUTHOR(S): WOJTCZAK L [Reprint author]; CHRISTIANSEN E N; ZBOROWSKI J
CORPORATE SOURCE: NENCKI INST EXP BIOL, WARSAW 02-093, POL
SOURCE: Comparative Biochemistry and Physiology B, (1980) Vol. 66, No. 2, pp. 241-248.
CODEN: CBPBB8. ISSN: 0305-0491.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Mitochondria isolated from the interscapular brown **adipose** tissue of cold-adapted guinea pig incorporate glycerol 3-phosphate labeled with 14C or 32P into lysophosphatidic and phosphatidic acids and, to a lower extent, into cardiolipin. This process requires ATP and is potentiated by addition of CoA. In mitochondria depleted of endogenous fatty acids by washing with serum albumin, addition of a fatty acid is also required. In mitochondria depleted of endogenous fatty acids and subsequently supplemented with palmitate or oleate, the incorporation into tentatively identified phosphatidylglycerol is greatly enhanced. Labeled fatty acids are incorporated into phosphatidic and lysophosphatidic acids, phosphatidylcholine and phosphatidylethanolamine. In the absence of glycerol 3-phosphate, the 2 latter phospholipids are the only labeled compounds formed, pointing to the acylation of lysophospholipids.

L8 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1979:141465 BIOSIS
DOCUMENT NUMBER: PREV197967021465; BA67:21465
TITLE: MITOCHONDRIAL THYROID HORMONE RECEPTOR LOCALIZATION AND PHYSIOLOGICAL SIGNIFICANCE.
AUTHOR(S): STERLING K [Reprint author]; LAZARUS J H; MILCH P O; SAKURADA T; BRENNER M A
CORPORATE SOURCE: DEP MED, COLUMBIA UNIV COLL PHYSICIANS SURG, BRONX, NY 10468, USA
SOURCE: Science (Washington D C), (1978) Vol. 201, No. 4361, pp. 1126-1129.
CODEN: SCIEAS. ISSN: 0036-8075.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Binding studies of thyroid hormone to submitochondrial fractions from rat liver suggest that the component responsible for high-affinity, low-capacity (saturable) binding of hormones arises from the inner mitochondrial membrane. The partially purified component, approximately 150,000 daltons, appears to be half protein and half lipid, largely phospholipids, tentatively identified as lecithin, phosphatidyl ethanolamine and cardiolipin. A similar hormone-binding macromolecule was found in mitochondria from rabbit kidney, from human liver and kidney, and from rat kidney, myocardium, skeletal muscle, intestinal mucosa, whole small intestine, **adipose** tissue and lung. It was absent from mitochondria of adult rat brain, spleen, and testis, organs calorigenically unresponsive to thyroid hormones infected in vivo, but was present in mitochondria from brains of rats 12 days old and younger. The organ distribution of the hormone-binding protein and its presence in neonatal brain mitochondria supports the biological relevance of the mitochondrial component as a thyroid hormone receptor.

=> d his

(FILE 'HOME' ENTERED AT 13:39:34 ON 30 JAN 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS' ENTERED AT 13:39:56 ON 30 JAN 2004
L1 384 S REUE K?/AU OR PETERFY M?/AU

```
L2            14 S L1 AND (LPIN OR LIPIN)
L3             8 DUP REM L2 (6 DUPLICATES REMOVED)
L4          1086 S (LIPIN OR LPIN)
L5             9 S L4 AND (GENE EXPRESSION)
L6             7 DUP REM L5 (2 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 13:45:52 ON 30 JAN 2004

     FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
     ENTERED AT 13:47:49 ON 30 JAN 2004
L7            16 S L4 AND ADIPOSE
L8            10 DUP REM L7 (6 DUPLICATES REMOVED)

=> s l4 and mRNA
L9             9 L4 AND MRNA

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10            4 DUP REM L9 (5 DUPLICATES REMOVED)

=> d ibib abs l10 1-4

L10  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:212043  CAPLUS
DOCUMENT NUMBER:          138:383344
TITLE:                    Gene expression profiles of nondiabetic and diabetic
                          obese mice suggest a role of hepatic lipogenic
                          capacity in diabetes susceptibility
AUTHOR(S):                Lan, Hong; Rabaglia, Mary E.; Stoehr, Jonathan P.;
                          Nadler, Samuel T.; Schueler, Kathryn L.; Zou, Fei;
                          Yandell, Brian S.; Attie, Alan D.
CORPORATE SOURCE:         Department of Biochemistry, University of Wisconsin,
                          Madison, WI, 53706, USA
SOURCE:                   Diabetes (2003), 52(3), 688-700
                          CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER:                American Diabetes Association
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Obesity is a strong risk factor for the development of type 2 diabetes.
     The authors have previously reported that in adipose tissue of obese
     (ob/ob) mice, the expression of adipogenic genes is decreased.  When made
     genetically obese, the BTBR mouse strain is diabetes susceptible and the
     C57BL/6J (B6) strain is diabetes resistant.  The authors used DNA
     microarrays and RT-PCR to compare the gene expression in BTBR-ob/ob vs.
     B6-ob/ob mice in adipose tissue, liver, skeletal muscle, and pancreatic
     islets.  The authors' results show: (1) there is an increased expression
     of genes involved in inflammation in adipose tissue of diabetic mice; (2)
     lipogenic gene expression was lower in adipose tissue of
     diabetes-susceptible mice, and it continued to decrease with the
     development of diabetes, compared with diabetes-resistant obese mice; (3)
     hepatic expression of lipogenic enzymes was increased and the hepatic
     triglyceride content was greatly elevated in diabetes-resistant obese
     mice; (4) hepatic expression of gluconeogenic genes was suppressed at the
     prediabetic stage but not at the onset of diabetes; and (5) genes normally
     not expressed in skeletal muscle and pancreatic islets were expressed in
     these tissues in the diabetic mice.  The authors propose that increased
     hepatic lipogenic capacity protects the B6-ob/ob mice from the development
     of type 2 diabetes.
REFERENCE COUNT:          41    THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10   ANSWER 2 OF 4  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-01876  BIOTECHDS
TITLE:            New mouse Lpin1 and human LPIN1 genes associated with
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adiposity/insulin response regulation, useful for screening agents that alter adipose tissue development, or for diagnosing a predilection to lipodystrophy, obesity or diabetes;
vector-mediated recombinant protein gene transfer and expression in host cell for use in diagnosis and therapy

AUTHOR: REUE K; PETERFY M
PATENT ASSIGNEE: UNIV CALIFORNIA
PATENT INFO: WO 2002059248 1 Aug 2002
APPLICATION INFO: WO 2001-US50237 20 Dec 2001
PRIORITY INFO: US 2000-257772 22 Dec 2000; US 2000-257772 22 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-599767 [64]
AN 2003-01876 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A isolated nucleic acid encoding a polypeptide consisting of human **lipin** 1A, mouse **lipin** 1A or mouse **lipin** 1B, having the mouse Lpin1 or human LPIN1 nucleic acid sequences, or hybridizing to them under stringent conditions, and encoding a **lipin** polypeptide, is new.

DETAILED DESCRIPTION - An isolated nucleic acid encoding the human **lipin** 1A, mouse **lipin** 1A or mouse **lipin** 1B polypeptides, which comprises a 890, 891 or 924 residue amino acid sequence, respectively, given in the specification. The mouse Lpin1 nucleic acid comprises a 5175 base pair sequence, given in the specification. The human LPIN1 nucleic acid comprises a 5248 base pair sequence, given in the specification. The primers comprise the following sequences: Primer 1: 5'-CAGACAATGAATTACGTGGGGCAGCT-3' Primer 2: 5'-GCTGAGGCTGAATGCATGTCCTGGT-3' Primer 3: 5'-CCATGAATTACGTGGGGCAG-3' Primer 4: 5'-CGCTGAGGCAGAATGAATGTC-3'. INDEPENDENT CLAIMS are also included for the following: (1) (pre)screening an agent that alters adipose tissue development; (2) a polypeptide encoded by the nucleic acid, or an isolated **lipin** polypeptide comprising a polypeptide that comprises an NLIP domain and a CLIP domain; (3) a transgenic animal comprising a recombinantly modified Lpin1/LPIN1 gene, so that the recombinantly modified gene does not transcribe a functional **lipin** protein; (4) identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis; (5) mitigating a symptom of lipodystrophy, obesity, diabetes, atherosclerosis, or related pathology; and (6) inhibiting fat accumulation in a mammal by inhibiting **lipin** expression or activity.

BIOTECHNOLOGY - Preferred Nucleic Acid: The nucleic acid is at least 15 nucleotides in length. The **lipin** polypeptide encoded by the new nucleic acid has a NLIP domain that comprises the consensus sequence of 86 or 159 amino acids defined in the specification. Preferred Antibody: The antibody is a single-chain antibody or a polyclonal antibody. Preferred Animal: The transgenic animal is homozygous for the recombinantly modified Lpin1/LPIN1 gene. The animal is a murine or a mouse. This transgenic animal is chimeric for cells comprising the recombinantly modified Lpin1/LPIN1 gene. Preferred Method: In method (1), screening for an agent that alters adipose tissue development comprises: (a) contacting a cell comprising a Lpin1 gene with a test agent; and (b) detecting a change in the expression or activity of the Lpin1 gene product as compared to the expression or activity of a Lpin1 gene product in a cell that is contacted with the test agent at a lower concentration. A difference in the expression or activity of **lipin** in the contacted cell and control cell with the lower concentration indicates that the agent alters adipose tissue development. The lower concentration is the absence of the test agent. The cell is cultured ex vivo, and the test agent is contacted to an animal comprising a cell containing the Lpin1 gene nucleic acid or **lipin** protein. Prescreening for an agent that alters adipose tissue development comprises: (a) contacting a

Lpin1 nucleic acid or a **lipin** protein with a test agent; and (b) detecting specific binding of the test agent to the **lipin** protein or nucleic acid. The method further comprises recording test agents that specifically bind to the Lpin1 nucleic acid or protein in a database of candidate agents that alter adipose tissue development. Preferably, the test agent is not an antibody, not a protein, and not a nucleic acid. The test agent is preferably a small organic molecule. The detecting comprises detecting specific binding of the test agent to the Lpin1 nucleic acid. Detecting specific binding of the test agent to the **lipin** protein is preferably via capillary electrophoresis, a Western blot, mass spectroscopy, enzyme linked immunosorbent assay (ELISA), immunochromatography, or immunohistochemistry. The test agent is contacted directly to the Lpin1 nucleic acid or to the **lipin** protein. The test agent may also be contacted to a cell or to an animal comprising a cell containing the Lpin1 nucleic acid or the **lipin** protein, where the cell is cultured ex vivo. In method (4), identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis comprises: (a) obtaining a biological sample from the organism; and (b) detecting a LPIN1 gene product, where a difference in the amount or activity of the LPIN1 gene product from the organism as compared to a gene product from a normal healthy organism indicates that the organism has or is susceptible to a lipodystrophic phenotype, obesity, diabetes, atherosclerosis or related pathology. In the methods above, the amount of Lpin1 or LPIN1 gene product is detected by detecting Lpin1 **mRNA** in the sample or LPIN1 **mRNA** in a cell. The level of Lpin1 or LPIN1 **mRNA** is measured by hybridizing the **mRNA** to a probe that specifically hybridizes to a Lpin1 or LPIN1 nucleic acid, or by using a nucleic acid amplification reaction. The amount of Lpin1 or LPIN1 gene product is detected by detecting the level of a **lipin** protein in the biological sample, preferably via a method comprising capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, or immunohistochemistry. The method may also comprise: (a) obtaining a biological sample from the organism; and (b) detecting a mutation in a Lpin1/LPIN1 gene or gene product from the biological sample. The mutation may be an insertion, a deletion, a missense point mutation or a nonsense point mutation. Detecting is by a method comprising Southern blot, DNA amplification, comparative genomic hybridization, immunohistochemistry or cytogenetics. Detection may also involve detecting a mutation in a polypeptide by capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, or immunohistochemistry. In all the methods above, binding is detected or hybridization is according to method selected from Northern blot, southern blot using DNA derived from the Lpin1 RNA, an array hybridization, an affinity chromatography, and an in situ hybridization. In method (5), mitigating a symptom of lipodystrophy, obesity, diabetes, atherosclerosis, or related pathology comprises modulating the concentration and/or activity of a LPIN1 gene product in a cell of an organism, particularly by upregulating or repressing expression of heterologous or endogenous LPIN1 nucleic acid. Modulation involves transfecting the cell with a vector that expresses a **lipin** protein, where the vector constitutively expresses a **lipin** protein. The expression of the **lipin** protein by the vector is either inducible or constitutive. Preferably, the cell is an adipocyte. In method (6), inhibiting fat accumulation in a mammal comprises: (a) contacting a **lipin** nucleic acid with a ribozyme that specifically cleaves the **lipin** nucleic acid; (b) contacting a **lipin** nucleic acid with a catalytic DNA that specifically cleaves the **lipin** nucleic acid; (c) transfecting a cell comprising a **lipin** gene with a nucleic acid that inactivates the **lipin** gene by homologous recombination with the **lipin** gene; (d) transfecting a cell with a nucleic acid encoding an intrabody that specifically binds a **lipin** polypeptide; or (e) transfecting the cell with a **lipin** antisense molecule.

Preferred Probe: The probe is a member of several probes that form an array of probes.

ACTIVITY - Antilipemic; Anorectic; Antidiabetic; Antiarteriosclerotic. No biological data is given.

MECHANISM OF ACTION - Lipin1 Modulator; LIPIN1 Modulator; **Lipin** Inhibitor.

USE - The nucleic acid molecules useful for screening agents that alter adipose tissue development, or for diagnosing or identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis (claimed). The agents obtained are useful for inhibiting fat accumulation in a mammal, or for regulating adiposity and insulin response.

ADMINISTRATION - Dosage is 1-10000, preferably 10-100 micro-g. Administration of **lipin** inhibitors is parenteral, intravenous, topical, oral or local.

EXAMPLE - Northern blot analysis of total RNA from wild type mouse tissue revealed that **lipin mRNA** was expressed in adipose tissue, skeletal muscle and testis. Results showed that Lpin1 encoded a gene product of 891 amino acids. Database searches identified several mouse and human expressed sequence tag (EST)s and genomic sequences with significant similarities to Lpin1. It was also found that the human ortholog of the Lpin1, LPIN1, comprised 5248 base pairs. (87 pages)

L10 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:713426 CAPLUS

DOCUMENT NUMBER: 138:51181

TITLE: Paraquat-induced gene expression in rat lung tissues using a differential display reverse transcription-polymerase chain reaction

AUTHOR(S): Tomita, Masafumi; Nohno, Tsutomu; Okuyama, Toshiko; Nishimatsu, Shin-ichiro; Adachi, Junko

CORPORATE SOURCE: Department of Legal Medicine, Kawasaki Medical School, Kurashiki, 701-0192, Japan

SOURCE: Archives of Toxicology (2002), 76(9), 530-537
CODEN: ARTODN; ISSN: 0340-5761

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Increased formation of reactive oxygen species is a cause of paraquat (PQ)-induced injury and also provides a link between the signaling pathways and transcriptional events that regulate the expression of a large no. of genes. However, the mol. mechanisms involved in PQ-induced injury remain unclear. To investigate the changes in gene expression at the onset of PQ injury, the authors used the differential display-polymerase chain reaction (PCR) method. Rats were treated i.p. with 20 mg/kg PQ, and after 3 h the lungs were immediately excised. Samples of **mRNA** from normal and treated rats were used to prep. radiolabeled cDNAs, which were electrophoresed. Then the transcription levels were compared. The authors isolated 26 fragments of cDNA that were potentially affected by PQ, and detd. their nucleotide sequences. Six clones of interest were selected and analyzed further. The reverse transcript-PCR based on their sequence information confirmed the differential expression for five clones: four clones were up-regulated and one was down-regulated. The authors were particularly interested in two genes that had homol. with the known gene: TATA box-binding protein-assocd. factor, RNA polymerase II, B, 150 kDa (TAFIIB), and a candidate gene for lipodystrophy, Lpin2. Both genes were significantly up-regulated within 3 h of PQ intake and the stimulation continued during our 24-h observation period. In addn., up-regulation of Lpin2 was obsd. in the lungs, but not in the liver and kidneys. In situ hybridization using lung sections showed that the expression of both genes was strongly visualized in Clara cells and in alveolar macrophages. These findings suggest a stimulation of transcription levels and changes in lipid metab.

in Clara cells and in macrophages in the lungs, which result in their playing a crucial role at the onset of PQ-driven pulmonary injury.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001099615 MEDLINE
DOCUMENT NUMBER: 20578762 PubMed ID: 11138012
TITLE: Lipodystrophy in the fld mouse results from mutation of a new gene encoding a nuclear protein, **lipin**.
AUTHOR: Peterfy M; Phan J; Xu P; Reue K
CORPORATE SOURCE: Department of Medicine, University of California, Los Angeles, California, USA.
CONTRACT NUMBER: HL24841 (NHLBI)
SOURCE: NATURE GENETICS, (2001 Jan) 27 (1) 121-4.
Journal code: 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF180471; GENBANK-AF286724; GENBANK-AL132654; GENBANK-P32567; GENBANK-Q14693; GENBANK-Q92539
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB Mice carrying mutations in the fatty liver dystrophy (fld) gene have features of human lipodystrophy, a genetically heterogeneous group of disorders characterized by loss of body fat, fatty liver, hypertriglyceridemia and insulin resistance. Through positional cloning, we have isolated the gene responsible and characterized two independent mutant alleles, fld and fld(2J). The gene (Lpin1) encodes a novel nuclear protein which we have named **lipin**. Consistent with the observed reduction of adipose tissue mass in fld and fld(2J)mice, wild-type Lpin1 **mRNA** is expressed at high levels in adipose tissue and is induced during differentiation of 3T3-L1 pre-adipocytes. Our results indicate that **lipin** is required for normal adipose tissue development, and provide a candidate gene for human lipodystrophy. **Lipin** defines a novel family of nuclear proteins containing at least three members in mammalian species, and homologs in distantly related organisms from human to yeast.

=> d his

(FILE 'HOME' ENTERED AT 13:39:34 ON 30 JAN 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 13:39:56 ON 30 JAN 2004
L1 384 S REUE K?/AU OR PETERFY M?/AU
L2 14 S L1 AND (LPIN OR LIPIN)
L3 8 DUP REM L2 (6 DUPLICATES REMOVED)
L4 1086 S (LIPIN OR LPIN)
L5 9 S L4 AND (GENE EXPRESSION)
L6 7 DUP REM L5 (2 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 13:45:52 ON 30 JAN 2004

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 13:47:49 ON 30 JAN 2004
L7 16 S L4 AND ADIPOSE
L8 10 DUP REM L7 (6 DUPLICATES REMOVED)
L9 9 S L4 AND MRNA
L10 4 DUP REM L9 (5 DUPLICATES REMOVED)

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=> s l4 and screen?
L11          17 L4 AND SCREEN?

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12          16 DUP REM L11 (1 DUPLICATE REMOVED)

=> d ibib abs l12 1-16

L12   ANSWER 1 OF 16  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-01876  BIOTECHDS
TITLE:            New mouse Lpin1 and human LPIN1 genes associated with
                  adiposity/insulin response regulation, useful for
                  screening agents that alter adipose tissue
                  development, or for diagnosing a predilection to
                  lipodystrophy, obesity or diabetes;
                     vector-mediated recombinant protein gene transfer and
                     expression in host cell for use in diagnosis and therapy
AUTHOR:           REUE K; PETERFY M
PATENT ASSIGNEE:  UNIV CALIFORNIA
PATENT INFO:      WO 2002059248 1 Aug 2002
APPLICATION INFO: WO 2001-US50237 20 Dec 2001
PRIORITY INFO:    US 2000-257772 22 Dec 2000; US 2000-257772 22 Dec 2000
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2002-599767 [64]
AN    2003-01876  BIOTECHDS
AB    DERWENT ABSTRACT:
      NOVELTY - A isolated nucleic acid encoding a polypeptide consisting of
      human lipin 1A, mouse lipin 1A or mouse lipin
      1B, having the mouse Lpin1 or human LPIN1 nucleic acid sequences, or
      hybridizing to them under stringent conditions, and encoding a
      lipin polypeptide, is new.
           DETAILED DESCRIPTION - An isolated nucleic acid encoding the human
      lipin 1A, mouse lipin 1A or mouse lipin 1B
      polypeptides, which comprises a 890, 891 or 924 residue amino acid
      sequence, respectively, given in the specification. The mouse Lpin1
      nucleic acid comprises a 5175 base pair sequence, given in the
      specification. The human LPIN1 nucleic acid comprises a 5248 base pair
      sequence, given in the specification. The primers comprise the following
      sequences: Primer 1: 5'-CAGACAATGAATTACGTGGGGCAGCT-3' Primer 2:
      5'-GCTGAGGCTGAATGCATGTCCTGGT-3' Primer 3: 5'-CCATGAATTACGTGGGGCAG-3'
      Primer 4: 5'-CGCTGAGGCAGAATGAATGTC-3'. INDEPENDENT CLAIMS are also
      included for the following: (1) (pre)screening an agent that
      alters adipose tissue development; (2) a polypeptide encoded by the
      nucleic acid, or an isolated lipin polypeptide comprising a
      polypeptide that comprises an NLIP domain and a CLIP domain; (3) a
      transgenic animal comprising a recombinantly modified Lpin1/LPIN1 gene,
      so that the recombinantly modified gene does not transcribe a functional
      lipin protein; (4) identifying a predilection to developing one
      or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis;
      (5) mitigating a symptom of lipodystrophy, obesity, diabetes,
      atherosclerosis, or related pathology; and (6) inhibiting fat
      accumulation in a mammal by inhibiting lipin expression or
      activity.
           BIOTECHNOLOGY - Preferred Nucleic Acid: The nucleic acid is at least
      15 nucleotides in length. The lipin polypeptide encoded by the
      new nucleic acid has a NLIP domain that comprises the consensus sequence
      of 86 or 159 amino acids defined in the specification. Preferred
      Antibody: The antibody is a single-chain antibody or a polyclonal
      antibody. Preferred Animal: The transgenic animal is homozygous for the
      recombinantly modified Lpin1/LPIN1 gene. The animal is a murine or a
      mouse. This transgenic animal is chimeric for cells comprising the
```

recombinantly modified Lpin1/LPIN1 gene. Preferred Method: In method (1), **screening** for an agent that alters adipose tissue development comprises: (a) contacting a cell comprising a Lpin1 gene with a test agent; and (b) detecting a change in the expression or activity of the Lpin1 gene product as compared to the expression or activity of a Lpin1 gene product in a cell that is contacted with the test agent at a lower concentration. A difference in the expression or activity of **lipin** in the contacted cell and control cell with the lower concentration indicates that the agent alters adipose tissue development. The lower concentration is the absence of the test agent. The cell is cultured ex vivo, and the test agent is contacted to an animal comprising a cell containing the Lpin1 gene nucleic acid or **lipin** protein. Prescreening for an agent that alters adipose tissue development comprises: (a) contacting a Lpin1 nucleic acid or a **lipin** protein with a test agent; and (b) detecting specific binding of the test agent to the **lipin** protein or nucleic acid. The method further comprises recording test agents that specifically bind to the Lpin1 nucleic acid or protein in a database of candidate agents that alter adipose tissue development. Preferably, the test agent is not an antibody, not a protein, and not a nucleic acid. The test agent is preferably a small organic molecule. The detecting comprises detecting specific binding of the test agent to the Lpin1 nucleic acid. Detecting specific binding of the test agent to the **lipin** protein is preferably via capillary electrophoresis, a Western blot, mass spectroscopy, enzyme linked immunosorbent assay (ELISA), immunochromatography, or immunohistochemistry. The test agent is contacted directly to the Lpin1 nucleic acid or to the **lipin** protein. The test agent may also be contacted to a cell or to an animal comprising a cell containing the Lpin1 nucleic acid or the **lipin** protein, where the cell is cultured ex vivo. In method (4), identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis comprises: (a) obtaining a biological sample from the organism; and (b) detecting a LPIN1 gene product, where a difference in the amount or activity of the LPIN1 gene product from the organism as compared to a gene product from a normal healthy organism indicates that the organism has or is susceptible to a lipodystrophic phenotype, obesity, diabetes, atherosclerosis or related pathology. In the methods above, the amount of Lpin1 or LPIN1 gene product is detected by detecting Lpin1 mRNA in the sample or LPIN1 mRNA in a cell. The level of Lpin1 or LPIN1 mRNA is measured by hybridizing the mRNA to a probe that specifically hybridizes to a Lpin1 or LPIN1 nucleic acid, or by using a nucleic acid amplification reaction. The amount of Lpin1 or LPIN1 gene product is detected by detecting the level of a **lipin** protein in the biological sample, preferably via a method comprising capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, or immunohistochemistry. The method may also comprise: (a) obtaining a biological sample from the organism; and (b) detecting a mutation in a Lpin1/LPIN1 gene or gene product from the biological sample. The mutation may be an insertion, a deletion, a missense point mutation or a nonsense point mutation. Detecting is by a method comprising Southern blot, DNA amplification, comparative genomic hybridization, immunohistochemistry or cytogenetics. Detection may also involve detecting a mutation in a polypeptide by capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, or immunohistochemistry. In all the methods above, binding is detected or hybridization is according to method selected from Northern blot, southern blot using DNA derived from the Lpin1 RNA, an array hybridization, an affinity chromatography, and an in situ hybridization. In method (5), mitigating a symptom of lipodystrophy, obesity, diabetes, atherosclerosis, or related pathology comprises modulating the concentration and/or activity of a LPIN1 gene product in a cell of an organism, particularly by upregulating or repressing expression of heterologous or endogenous LPIN1 nucleic acid. Modulation involves transfecting the cell with a vector that expresses a

lipin protein, where the vector constitutively expresses a **lipin** protein. The expression of the **lipin** protein by the vector is either inducible or constitutive. Preferably, the cell is an adipocyte. In method (6), inhibiting fat accumulation in a mammal comprises: (a) contacting a **lipin** nucleic acid with a ribozyme that specifically cleaves the **lipin** nucleic acid; (b) contacting a **lipin** nucleic acid with a catalytic DNA that specifically cleaves the **lipin** nucleic acid; (c) transfecting a cell comprising a **lipin** gene with a nucleic acid that inactivates the **lipin** gene by homologous recombination with the **lipin** gene; (d) transfecting a cell with a nucleic acid encoding an intrabody that specifically binds a **lipin** polypeptide; or (e) transfecting the cell with a **lipin** antisense molecule. Preferred Probe: The probe is a member of several probes that form an array of probes.

ACTIVITY - Antilipemic; Anorectic; Antidiabetic; Antiarteriosclerotic. No biological data is given.

MECHANISM OF ACTION - Lipin1 Modulator; LIPIN1 Modulator; **Lipin** Inhibitor.

USE - The nucleic acid molecules useful for **screening** agents that alter adipose tissue development, or for diagnosing or identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis (claimed). The agents obtained are useful for inhibiting fat accumulation in a mammal, or for regulating adiposity and insulin response.

ADMINISTRATION - Dosage is 1-10000, preferably 10-100 micro-g. Administration of **lipin** inhibitors is parenteral, intravenous, topical, oral or local.

EXAMPLE - Northern blot analysis of total RNA from wild type mouse tissue revealed that **lipin** mRNA was expressed in adipose tissue, skeletal muscle and testis. Results showed that Lpin1 encoded a gene product of 891 amino acids. Database searches identified several mouse and human expressed sequence tag (EST)s and genomic sequences with significant similarities to Lpin1. It was also found that the human ortholog of the Lpin1, LPIN1, comprised 5248 base pairs. (87 pages)

L12 ANSWER 2 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1997:510488 BIOSIS
DOCUMENT NUMBER: PREV199799809691
TITLE: Lignin degradation and in vitro digestibility of wheat straw treated with Brazilian tropical species of white rot fungi.
AUTHOR(S): Capelari, M. [Reprint author]; Zadrazil, F.
CORPORATE SOURCE: Inst. Botanica, Secretaria Meio Ambiente, Caixa Postal 4005, 01061-970, Sao Paulo, SP, Brazil
SOURCE: Folia Microbiologica, (1997) Vol. 42, No. 5, pp. 481-487. CODEN: FOMIAZ. ISSN: 0015-5632.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1997
Last Updated on STN: 10 Dec 1997

AB Brazilian tropical fungi were **screened** for lignin degradation, and the ability to increase or decrease the in vitro digestibility and pH of wheat straw used as a substrate (at 25 and 30 degree C after 30 and 60 d of incubation). Out of 72 species and strains of Agrocybe, Antrodiella, Auricularia, Coriolopsis, Cymatoderma, Fomitopsis, Ganoderma, Gerronema, Gloeophyllum, Gymnopilus, Irpex, Lentinus, Melanoporia, Oligoporus, Oudemansiella, Panaeolus, Peniophora, Phellinus, Pleurotus, Psathyrella, Psilocybe, Pycnoporus, Rigidoporus, Schizophyllum, Trametes, Trichaptum and Tyromyces, 22 decomposed more than 50% of **lipin** and 10 increased the in vitro substrate digestibility by more than 30 U. The highest degradation of lignin was observed with Lentinus crinitus (80%, 60 d) and the highest increase in in vitro substrate digestibility was caused by Peniophora utriculosa (36 U, 30 d).

L12 ANSWER 3 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:34294 BIOSIS
DOCUMENT NUMBER: PREV199799340697
TITLE: Comparative studies of lignin peroxidases and manganese-dependent peroxidases produced by selected white rot fungi in solid media.
AUTHOR(S): Zhao, Jiong; De Koker, Theodorus H.; Janse, Bernard J. H. [Reprint author]
CORPORATE SOURCE: Dep. Microbiol., Univ. Stellenbosch, Stellenbosch 7600, South Africa
SOURCE: FEMS Microbiology Letters, (1996) Vol. 145, No. 3, pp. 393-399.
CODEN: FMLED7. ISSN: 0378-1097.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997

AB The effect of various incubation conditions and media composition on ligninolytic activity by selected strains of white-rot fungi was determined in solid media. When compared to conventional methods using liquid media or woody substrates, this method is fast, simple and also quantitative. Manganese-dependent peroxidase was easily detected in all strains studied. However, detection of **lipin** peroxidase required optimisation of both growth medium and enzyme assay conditions. Using this method, we showed that the role of nitrogen and oxygen in ligninolytic activity varies and that conditions must be optimised for each individual even within the same species. Furthermore, several white rot fungi produced manganese-dependent peroxidase during the primary growth phase.

L12 ANSWER 4 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:331199 BIOSIS
DOCUMENT NUMBER: PREV198478067679; BA78:67679
TITLE: A COMPARISON OF SEROLOGIC REACTIVITY AMONG SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH OR WITHOUT ANTI RO SS-A ANTIBODIES.
AUTHOR(S): BELL D A [Reprint author]; KOMAR R; CHODIRKER W B; BLOCK J; CAIRNS E
CORPORATE SOURCE: DEP MED, UNIV HOSP, PO BOX 5339, STATION A, LONDON, ON, N6A 5A5, UK
SOURCE: Journal of Rheumatology, (1984) Vol. 11, No. 3, pp. 315-317.
CODEN: JRHUA9. ISSN: 0315-162X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The serum from 112 patients with systemic lupus erythematosus (SLE) was examined to compare serologic reactivity among anti-Ro positive and anti-Ro negative patients. While hypergammaglobulinemia, rheumatoid factor (RF) and elevated Clq [complement component 1q] binding were significantly more frequent among the anti-Ro positive group there was no increase in the frequency of anti-dsDNA [double stranded DNA] antibody measured by the Farr assay or antibodies to ssDNA, dsDNA, poly dG .cntdot. poly dC, poly (dA-dT) and cardiolipin measured by ELISA [enzyme-linked immunosorbent assay]. Patients with the highest levels of anti-DNA antibody by the Farr assay did not have any increased frequency of anti-Ro antibodies. Anti-Ro and anti-DNA antibodies are apparently independently regulated. The frequent occurrence of RF in anti-Ro positive SLE patient may provide a useful **screening** assay for this autoantibody among pregnant SLE patients.

L12 ANSWER 5 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:356115 BIOSIS

DOCUMENT NUMBER: PREV198478092595; BA78:92595
TITLE: REACTIONS OF THE EXTRACTS OF REITER TREPONEME WITH SYPHILITIC AND NONSYPHILITIC HUMAN SERA IN THE SINGLE RADIAL HEMOLYSIS TECHNIQUE.
AUTHOR(S): AL-QUDAH A A [Reprint author]; MOSTRATOS A
CORPORATE SOURCE: DEP BACTERIOL VIROL, MED SCH, UNIV MANCHESTER, OXFORD ROAD, MANCHESTER M13 9PT, UK
SOURCE: Journal of Medical Microbiology, (1984) Vol. 17, No. 3, pp. 273-282.
CODEN: JMMIAV. ISSN: 0022-2615.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB A single radial hemolysis (SRH) technique, using Reiter protein or Reiter lysate as the coating antigen, was investigated. Results obtained with syphilitic and presumed non-syphilitic human sera were compared with results obtained in the absorbed fluorescent treponemal antibody test (FTA-ABS), the Reiter protein complement fixation test (RPCFT), the Veneral Diseases Research Laboratory Slide test (VDRL) and the Cardiolipin Wasserman reaction (CWR). The SRH reaction, with either Reiter antigen, was more sensitive than any of the **screening** tests (RPCFT, VDRL and CWR) for detecting positive syphilitic antibodies. Although the SRH test used almost the same materials as the RPCFT, it was appreciably more sensitive for the detection of the group-specific antibodies in syphilitic human serum.

L12 ANSWER 6 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:240562 BIOSIS
DOCUMENT NUMBER: PREV198477073546; BA77:73546
TITLE: ISOLATION AND PARTIAL CHARACTERIZATION OF A CERULENIN SENSITIVE MUTANT OF PSEUDOMONAS-AERUGINOSA.
AUTHOR(S): KAWAHARA K [Reprint author]; UCHIDA K; AIDA K
CORPORATE SOURCE: INST APPLIED MICROBIOL, UNIV TOKYO, BUNKYO-KU, TOKYO 113, JAPAN
SOURCE: Journal of Antibiotics (Tokyo), (1983) Vol. 36, No. 10, pp. 1329-1335.
CODEN: JANTAJ. ISSN: 0021-8820.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB P. aeruginosa was resistant to cerulenin. Cerulenin-sensitive mutants were isolated from P. aeruginosa PML 1552 by 1-methyl-3-nitro-1-nitrosoguanidine treatment and following carbenicillin plus D-cycloserine **screening**. Isolated mutants were designated CSM-1 to CSM-19; some characteristics of CSM-19, which grew almost as well as the parent strain in the absence cerulenin, were examined. Growth of CSM-19 was greatly inhibited by 50 .mu.g/ml of cerulenin, but when a mixture of cellular fatty acids or both cis-vaccenic acid and palmitic acid were added to the medium, growth recovered partially. Incorporation of radioactivity into fatty acids from [1-14C]acetate was lowered by cerulenin. Thus, fatty acid synthesis by CSM-19 was decreased by cerulenin. Although cellular fatty acid composition and amount were not notably different between CSM-19 and PML 1552, CSM-19 had less phosphatidylethanolamine and more phosphatidylglycerol and cardiolipin than PML 1552. CSM-19 was also very sensitive to several other antibiotics, especially carbenicillin and tetracycline, when compared with PML 1552; the strains showed identical sensitivity to D-cycloserine, polymyxin B and chloramphenicol.

L12 ANSWER 7 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:315093 BIOSIS
DOCUMENT NUMBER: PREV198478051573; BA78:51573
TITLE: DEMONSTRATION OF LE-A ANTIGEN ON PLATELETS BY MEANS OF A MICRO TECHNIQUE OF PLATELET COMPLEMENT FIXATION.
AUTHOR(S): ANDO B [Reprint author]

CORPORATE SOURCE: CENTRAL CLIN LAB, KYUSU UNIV HOSP, FUKUOKA 812, JPN
SOURCE: Fukuoka Acta Medica, (1983) Vol. 74, No. 12, pp. 813-824.
CODEN: FKIZA4. ISSN: 0016-254X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: JAPANESE

AB Two anti-Lea antisera that reacted with platelets of donors having red cell phenotype Le (a+b-) were found in a **screening** of anti-platelet antibody in patients' sera, by a microcomplement fixation test. The complement fixation titer and hemagglutinin titer (2 stage anti-globulin test) of 1 serum were 32 and 32, and of another one were 16 and 8, respectively. The anti-Lea activity was completely absorbed by red cells, platelets and lymphocytes of donors having red cell phenotype Le (a+b-), but not by cells of Le (a-b+) or Le (a-b-) donors. The antibody activity against red cells was abolished by treatment of the antisera with DTT [dithiothreitol], suggesting that the activity resided in IgM-class Ig. As the anti-Lea was more reactive at 37.degree. C than at room temperature, not only against red cells but also against platelets, it was suggested that platelet transfusion of Lea negative donors should be indicated when patients had this kind of anti-Lea. When platelets of Le (a-) donors were incubated with plasma from Le (a+) donors in vitro, the Le (a-) platelets began to react with the anti-Lea anti-platelet sera. Lea antigen on platelets is probably derived from Lea substance in plasma, as is Lea antigen on erythrocytes. Although the Lea antigen in plasma could not be detected by complement fixation test, the fact that the antigen could be detected on platelets may be due to: adsorption of Lea antigen on platelets, and rearrangement of the antigen on platelets in such a way that IgM anti-Lea can initiate complement fixation. Cardiolipin, known as a monovalent antigen like Lea antigen in plasma, can not be detected efficiently by complement fixation test without formation of a liposome that consists of cardiolipin and lecithin. When cardiolipin was adsorbed on the platelet, it became detectable by complement fixation test. The platelet seems to be a natural matrix for liposome formation that is useful for complement fixation test.

L12 ANSWER 8 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:38218 BIOSIS
DOCUMENT NUMBER: PREV198426038218; BR26:38218
TITLE: THE EVOLUTION OF THE FLOCCULATION **SCREENING** TEST FOR SYPHILIS.
AUTHOR(S): KAMPMEIER R H [Reprint author]
CORPORATE SOURCE: VANDERBILT UNIV SCH MED, STATION 17, NASHVILLE, TENN 37232, USA
SOURCE: Sexually Transmitted Diseases, (1983) Vol. 10, No. 3, pp. 156-159.
ISSN: 0148-5717.
DOCUMENT TYPE: Article
General Review; (Literature Review)
FILE SEGMENT: BR
LANGUAGE: ENGLISH

L12 ANSWER 9 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1983:261766 BIOSIS
DOCUMENT NUMBER: PREV198376019258; BA76:19258
TITLE: REITER HEM AGGLUTINATION TEST A **SCREENING** TEST FOR SYPHILIS.
AUTHOR(S): AL-QUDAH A A [Reprint author]; MOSTRATOS A
CORPORATE SOURCE: DEP BACTERIOL VIROL, UNIV MANCHESTER MED SCH, OXFORD ROAD, MANCHESTER M13 9PT, UK
SOURCE: British Journal of Venereal Diseases, (1982) Vol. 58, No. 5, pp. 281-285.
CODEN: BJVDAK. ISSN: 0007-134X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA

LANGUAGE: ENGLISH

AB Using an ultrasonicate of the Reiter treponeme as antigen, the Reiter hemagglutination test (RHA) was evaluated as a serological test for syphilis. Comparison of the results of the cardiolipin Wassermann reaction, Reiter protein complement-fixation test, the fluorescent treponemal antibody-adsorbed (FTA-ABS) test, the Treponema pallidum hemagglutination test (TPHA) (at dilutions of 1/16 and 1/80) and the Venereal Disease Research Laboratory test with those of the RHA showed that the RHA was sensitive (85.8%) and agreed well (85.8%) with the FTA-ABS test result. Simplicity, sensitivity, availability of the antigen and the very low cost of this test support its use as a 1st-time **screening** test for [human] syphilis.

L12 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1981:296635 BIOSIS
DOCUMENT NUMBER: PREV198172081619; BA72:81619
TITLE: SEARCH FOR ORGANIZATIONAL FORMS OF INTRODUCTION OF AN EXPRESS METHOD FOR SERO DIAGNOSIS OF SYPHILIS.
AUTHOR(S): OVCHINNIKOV N M [Reprint author]; REZNIKOVA L S; MILONOVA T I; STOYANOVA O A; NIKOL'SKAYA E P; FRISHMAN M P; TATSKAYA L S; KOMOV O P; FEDOROVICH E M; ET AL
CORPORATE SOURCE: DEP MICROBIOL, CENT RES INST DERMATOL-VENEROL, MINIST HEALTH USSR, MOSCOW, USSR
SOURCE: Vestnik Dermatologii i Venerologii, (1980) No. 4, pp. 25-29.
CODEN: VDVEAV. ISSN: 0042-4609.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: RUSSIAN

AB Two selective microprecipitation tests with cardiolipin antigen, plasma and inactivated serum should be used for serological **screening** for syphilis on subjects liable to prophylactic examinations. The test with plasma should be used in the place where the blood was collected. When the blood is to be shipped to a remote laboratory, it should be collected from the vein and the test should be done with inactivated serum. The express method should be performed by specially appointed and well-trained personnel. When positive results are obtained, examinations should be repeated using a set of standard serological tests, and the subject should be examined by a dermato-venereologist.

L12 ANSWER 11 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1978:258020 BIOSIS
DOCUMENT NUMBER: PREV197866070517; BA66:70517
TITLE: FUNCTION OF PHOSPHO LIPIDS IN ESCHERICHIA-COLI CHARACTERIZATION OF A MUTANT DEFICIENT IN CARDIO **LIPIN** SYNTHESIS.
AUTHOR(S): PLUSCHKE G [Reprint author]; HIROTA Y; OVERATH P
CORPORATE SOURCE: MAX-PLANCK-INST BIOL, 74 TUEBINGEN, W GER
SOURCE: Journal of Biological Chemistry, (1978) Vol. 253, No. 14, pp. 5048-5055.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB **Screening** of a collection of temperature-sensitive mutants of E. coli for defects in phospholipid metabolism led to the isolation of a mutant deficient in cardiolipin synthesis. The defective gene, named cls, is closely linked to the trp marker and maps at about Minute 27 on the E. coli chromosome. After transfer of cls to a defined genetic background by transduction, the mutant has the following properties as compared to an isogenic wild type. Exponentially growing cells show a reduction in cardiolipin content by a factor of at least 15 (< 0.2 mol % of the total phospholipids). A crude membrane fraction derived from the mutant is unable to synthesize cardiolipin from phosphatidylglycerol in vitro. The

mutant has no distinctive phenotype regarding its growth properties, membrane-associated respiratory functions, or the ability to insert its growth properties, membrane-associated respiratory functions, or the ability to insert bacteriophage M13 coat protein into the cell envelope. The cls mutation confers a 5 times reduction in the turnover of the phosphate moiety of phosphatidylglycerol.

L12 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1978:93289 BIOSIS
DOCUMENT NUMBER: PREV197815036789; BR15:36789
TITLE: A CARDIO **LIPIN** REAGENT FOR SYPHILIS **SCREENING** ON GROUPAMATIC.
AUTHOR(S): HAAHTI E; LEIKOLA J; AHO K
SOURCE: Revue Francaise de Transfusion et Immuno-Hematologie, (1978) Vol. 21, No. 2, pp. 523-532. CODEN: RFTID6. ISSN: 0338-4535.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable

L12 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1978:192787 BIOSIS
DOCUMENT NUMBER: PREV197866005284; BA66:5284
TITLE: PROTEIN LIPID INTERACTIONS IN CYTOCHROME OXIDASE FROM SACCHAROMYCES-CEREVISIAE EFFECTS OF DETERGENTS AND RECONSTITUTION OF ENZYME ACTIVITY BY PHOSPHO LIPIDS BY USING CHOLATE MEDIATED EXCHANGE.
AUTHOR(S): VIRJI M [Reprint author]; KNOWLES P F
CORPORATE SOURCE: TENOVUS RES LAB, SOUTHAMPTON GEN HOSP, SOUTHAMPTON SO9 4XY, ENGL, UK
SOURCE: Biochemical Journal, (1978) Vol. 169, No. 2, pp. 343-354. ISSN: 0264-6021.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Cytochrome oxidase, purified from the yeast S. cerevisiae, was shown to have associated phospholipid, cholate or detergent, which was varied by dialysis or (NH4)2SO4 precipitation of the protein. Cholate and the detergents Triton X-100 and Tween 80 were shown to differ in their ability to support enzyme activity. Changes in the Vmax but not the Km, for ferrocytochrome c as the cholate concentration was varied indicate that cholate increases the number of exposed active sites of the enzyme. Cholate was used to introduce chosen phospholipids into the lipid environment of yeast cytochrome oxidase. Kinetic studies clearly showed that cholate can mediate exchange of exogenous for endogenous phospholipid. All phospholipids **screened** supported activity up to the basal value for the unsubstituted enzyme, whereas mitochondrial phosphatidylethanolamine and various phosphatidylcholines (except 1,2-dipalmitoyl-sn-glycero-3-phosphocholine) produced enhanced activity. A detailed kinetic examination revealed that the major effect of phosphatidylethanolamine is to increase k+1, whereas the major effect of phosphatidylcholine is to increase k+2 in the minimal kinetic scheme; where E = enzyme, S = substrate and P = product: .**GRAPHIC**. Cardiolipin, although supporting activity, does not give any enhancement of k+1 or k+2 over the values for the cholate control. The relevance of these observations to protein-lipid interactions in cytochrome oxidase is discussed.

L12 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1976:206932 BIOSIS
DOCUMENT NUMBER: PREV197662036932; BA62:36932
TITLE: PHOSPHATIDYL SERINE SYNTHETASE MUTANTS OF ESCHERICHIA-COLI GENETIC MAPPING AND MEMBRANE PHOSPHO LIPID COMPOSITION.
AUTHOR(S): RAETZ C R H

SOURCE: Journal of Biological Chemistry, (1976) Vol. 251, No. 11, pp. 3242-3249.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable
AB Mutants of E. coli K-12 defective in CDP-diglyceride:L-serine phosphatidyltransferase (phosphatidylserine synthetase) can be isolated by a rapid autoradiographic **screening** assay. Four organisms of this kind are now characterized. The gene (designated pss) which is altered in these mutants is closely linked to the nadB locus near minute 49 on the E. coli chromosome. Strains carrying the pss-8 mutation do not grow at elevated temperatures and have low levels of an altered synthetase in cell extracts. An analysis of several hundred transductants and temperature-resistant revertants reveals that the pss-8 mutation is responsible both for the enzyme defect and for the phenotype. When a pss-8 mutant is shifted to the nonpermissive temperature, the cells stop dividing and form long filaments. After 3 h at 44.degree. C, the level of phosphatidylethanolamine drops from 66 to 32% (percentage of the total lipid P), while the combined levels of phosphatidylglycerol and cardiolipin rise from 34 to 68%.

L12 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1976:70729 BIOSIS
DOCUMENT NUMBER: PREV197612070729; BR12:70729
TITLE: USE OF AUTOMATED TREPONEMAL AND CARDIO **LIPIN** TESTS IN **SCREENING** FOR SYPHILIS.
AUTHOR(S): FADDA G; RONZONI M; MORA G
SOURCE: Annali Sclavo, (1975) Vol. 17, No. 2, pp. 209-214.
CODEN: ASCLAZ. ISSN: 0003-472X.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable

L12 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1974:95753 BIOSIS
DOCUMENT NUMBER: PREV197410095753; BR10:95753
TITLE: A NEW REAGIN CARD TEST FOR SYPHILIS.
AUTHOR(S): MARCH R W; STILES G E; MORGIONE P S
SOURCE: Abstracts of the Annual Meeting of the American Society for Microbiology, (1974) Vol. 74, pp. 93.
CODEN: ASMACK. ISSN: 0094-8519.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable

=> d his

(FILE 'HOME' ENTERED AT 13:39:34 ON 30 JAN 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS' ENTERED AT 13:39:56 ON 30 JAN 2004
L1 384 S REUE K?/AU OR PETERFY M?/AU
L2 14 S L1 AND (LPIN OR LIPIN)
L3 8 DUP REM L2 (6 DUPLICATES REMOVED)
L4 1086 S (LIPIN OR LPIN)
L5 9 S L4 AND (GENE EXPRESSION)
L6 7 DUP REM L5 (2 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 13:45:52 ON 30 JAN 2004

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS' ENTERED AT 13:47:49 ON 30 JAN 2004

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L7            16 S L4 AND ADIPOSE
L8            10 DUP REM L7 (6 DUPLICATES REMOVED)
L9             9 S L4 AND MRNA
L10            4 DUP REM L9 (5 DUPLICATES REMOVED)
L11           17 S L4 AND SCREEN?
L12           16 DUP REM L11 (1 DUPLICATE REMOVED)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L13         1045 DUP REM L4 (41 DUPLICATES REMOVED)

=> s l13 and (nucleic acid or probe or gene product)
L14           15 L13 AND (NUCLEIC ACID OR PROBE OR GENE PRODUCT)

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15           15 DUP REM L14 (0 DUPLICATES REMOVED)

=> d ibib abs l15 1-15

L15   ANSWER 1 OF 15  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-01876  BIOTECHDS
TITLE:            New mouse Lpin1 and human LPIN1 genes associated with
                  adiposity/insulin response regulation, useful for screening
                  agents that alter adipose tissue development, or for
                  diagnosing a predilection to lipodystrophy, obesity or
                  diabetes;
                     vector-mediated recombinant protein gene transfer and
                     expression in host cell for use in diagnosis and therapy
AUTHOR:           REUE K; PETERFY M
PATENT ASSIGNEE:  UNIV CALIFORNIA
PATENT INFO:      WO 2002059248 1 Aug 2002
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LANGUAGE:         English
OTHER SOURCE:     WPI: 2002-599767 [64]
AN    2003-01876  BIOTECHDS
AB    DERWENT ABSTRACT:
      NOVELTY - A isolated nucleic acid encoding a
      polypeptide consisting of human lipin 1A, mouse lipin
      1A or mouse lipin 1B, having the mouse Lpin1 or human LPIN1
      nucleic acid sequences, or hybridizing to them under
      stringent conditions, and encoding a lipin polypeptide, is new.
           DETAILED DESCRIPTION - An isolated nucleic acid
      encoding the human lipin 1A, mouse lipin 1A or mouse
      lipin 1B polypeptides, which comprises a 890, 891 or 924 residue
      amino acid sequence, respectively, given in the specification. The mouse
      Lpin1 nucleic acid comprises a 5175 base pair
      sequence, given in the specification. The human LPIN1 nucleic
      acid comprises a 5248 base pair sequence, given in the
      specification. The primers comprise the following sequences: Primer 1:
      5'-CAGACAATGAATTACGTGGGGCAGCT-3' Primer 2: 5'-GCTGAGGCTGAATGCATGTCCTGGT-
      3' Primer 3: 5'-CCATGAATTACGTGGGGCAG-3' Primer 4: 5'-
      CGCTGAGGCAGAATGAATGTC-3'. INDEPENDENT CLAIMS are also included for the
      following: (1) (pre)screening an agent that alters adipose tissue
      development; (2) a polypeptide encoded by the nucleic
      acid, or an isolated lipin polypeptide comprising a
      polypeptide that comprises an NLIP domain and a CLIP domain; (3) a
      transgenic animal comprising a recombinantly modified Lpin1/LPIN1 gene,
      so that the recombinantly modified gene does not transcribe a functional
      lipin protein; (4) identifying a predilection to developing one
      or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis;
      (5) mitigating a symptom of lipodystrophy, obesity, diabetes,
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atherosclerosis, or related pathology; and (6) inhibiting fat accumulation in a mammal by inhibiting **lipin** expression or activity.

BIOTECHNOLOGY - Preferred **Nucleic Acid**: The **nucleic acid** is at least 15 nucleotides in length. The **lipin** polypeptide encoded by the new **nucleic acid** has a NLIP domain that comprises the consensus sequence of 86 or 159 amino acids defined in the specification. Preferred Antibody: The antibody is a single-chain antibody or a polyclonal antibody. Preferred Animal: The transgenic animal is homozygous for the recombinantly modified Lpin1/LPIN1 gene. The animal is a murine or a mouse. This transgenic animal is chimeric for cells comprising the recombinantly modified Lpin1/LPIN1 gene. Preferred Method: In method (1), screening for an agent that alters adipose tissue development comprises: (a) contacting a cell comprising a Lpin1 gene with a test agent; and (b) detecting a change in the expression or activity of the Lpin1 **gene product** as compared to the expression or activity of a Lpin1 **gene product** in a cell that is contacted with the test agent at a lower concentration. A difference in the expression or activity of **lipin** in the contacted cell and control cell with the lower concentration indicates that the agent alters adipose tissue development. The lower concentration is the absence of the test agent. The cell is cultured ex vivo, and the test agent is contacted to an animal comprising a cell containing the Lpin1 gene **nucleic acid** or **lipin** protein. Prescreening for an agent that alters adipose tissue development comprises: (a) contacting a Lpin1 **nucleic acid** or a **lipin** protein with a test agent; and (b) detecting specific binding of the test agent to the **lipin** protein or **nucleic acid**. The method further comprises recording test agents that specifically bind to the Lpin1 **nucleic acid** or protein in a database of candidate agents that alter adipose tissue development. Preferably, the test agent is not an antibody, not a protein, and not a **nucleic acid**. The test agent is preferably a small organic molecule. The detecting comprises detecting specific binding of the test agent to the Lpin1 **nucleic acid**. Detecting specific binding of the test agent to the **lipin** protein is preferably via capillary electrophoresis, a Western blot, mass spectroscopy, enzyme linked immunosorbent assay (ELISA), immunochromatography, or immunohistochemistry. The test agent is contacted directly to the Lpin1 **nucleic acid** or to the **lipin** protein. The test agent may also be contacted to a cell or to an animal comprising a cell containing the Lpin1 **nucleic acid** or the **lipin** protein, where the cell is cultured ex vivo. In method (4), identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis comprises: (a) obtaining a biological sample from the organism; and (b) detecting a LPIN1 **gene product**, where a difference in the amount or activity of the LPIN1 **gene product** from the organism as compared to a **gene product** from a normal healthy organism indicates that the organism has or is susceptible to a lipodystrophic phenotype, obesity, diabetes, atherosclerosis or related pathology. In the methods above, the amount of Lpin1 or LPIN1 **gene product** is detected by detecting Lpin1 mRNA in the sample or LPIN1 mRNA in a cell. The level of Lpin1 or LPIN1 mRNA is measured by hybridizing the mRNA to a **probe** that specifically hybridizes to a Lpin1 or LPIN1 **nucleic acid**, or by using a **nucleic acid** amplification reaction. The amount of Lpin1 or LPIN1 **gene product** is detected by detecting the level of a **lipin** protein in the biological sample, preferably via a method comprising capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, or immunohistochemistry. The method may also comprise: (a) obtaining a biological sample from the organism; and (b) detecting a mutation in a

Lpin1/LPIN1 gene or **gene product** from the biological sample. The mutation may be an insertion, a deletion, a missense point mutation or a nonsense point mutation. Detecting is by a method comprising Southern blot, DNA amplification, comparative genomic hybridization, immunohistochemistry or cytogenetics. Detection may also involve detecting a mutation in a polypeptide by capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, or immunohistochemistry. In all the methods above, binding is detected or hybridization is according to method selected from Northern blot, southern blot using DNA derived from the Lpin1 RNA, an array hybridization, an affinity chromatography, and an in situ hybridization. In method (5), mitigating a symptom of lipodystrophy, obesity, diabetes, atherosclerosis, or related pathology comprises modulating the concentration and/or activity of a LPIN1 **gene product** in a cell of an organism, particularly by upregulating or repressing expression of heterologous or endogenous LPIN1 **nucleic acid**. Modulation involves transfecting the cell with a vector that expresses a **lipin** protein, where the vector constitutively expresses a **lipin** protein. The expression of the **lipin** protein by the vector is either inducible or constitutive. Preferably, the cell is an adipocyte. In method (6), inhibiting fat accumulation in a mammal comprises: (a) contacting a **lipin nucleic acid** with a ribozyme that specifically cleaves the **lipin nucleic acid**; (b) contacting a **lipin nucleic acid** with a catalytic DNA that specifically cleaves the **lipin nucleic acid**; (c) transfecting a cell comprising a **lipin** gene with a **nucleic acid** that inactivates the **lipin** gene by homologous recombination with the **lipin** gene; (d) transfecting a cell with a **nucleic acid** encoding an intrabody that specifically binds a **lipin** polypeptide; or (e) transfecting the cell with a **lipin** antisense molecule. Preferred **Probe**: The **probe** is a member of several probes that form an array of probes.

ACTIVITY - Antilipemic; Anorectic; Antidiabetic; Antiarteriosclerotic. No biological data is given.

MECHANISM OF ACTION - Lipin1 Modulator; LIPIN1 Modulator; **Lipin** Inhibitor.

USE - The **nucleic acid** molecules useful for screening agents that alter adipose tissue development, or for diagnosing or identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes or atherosclerosis (claimed). The agents obtained are useful for inhibiting fat accumulation in a mammal, or for regulating adiposity and insulin response.

ADMINISTRATION - Dosage is 1-10000, preferably 10-100 micro-g. Administration of **lipin** inhibitors is parenteral, intravenous, topical, oral or local.

EXAMPLE - Northern blot analysis of total RNA from wild type mouse tissue revealed that **lipin** mRNA was expressed in adipose tissue, skeletal muscle and testis. Results showed that Lpin1 encoded a **gene product** of 891 amino acids. Database searches identified several mouse and human expressed sequence tag (EST)s and genomic sequences with significant similarities to Lpin1. It was also found that the human ortholog of the Lpin1, LPIN1, comprised 5248 base pairs. (87 pages)

L15 ANSWER 2 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1990:355076 BIOSIS
DOCUMENT NUMBER: PREV199090051655; BA90:51655
TITLE: HORMONAL CONTROL OF HEMOLYMPH LIPOPROTEIN ICE NUCLEATORS IN OVERWINTERING FREEZE-SUSCEPTIBLE LARVAE OF THE STAG BEETLE CERUCHUS-PICEUS ADIPOKINETIC HORMONE AND JUVENILE HORMONE.
AUTHOR(S): XU L [Reprint author]; NEVEN L G; DUMAN J G
CORPORATE SOURCE: DEP BIOLOGICAL SCI, UNIV NOTRE DAME, NOTRE DAME, INDIANA

46556, USA
SOURCE: Journal of Comparative Physiology B Biochemical Systemic and Environmental Physiology, (1990) Vol. 160, No. 1, pp. 51-60.
CODEN: JPBPDL. ISSN: 0174-1578.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 7 Aug 1990
Last Updated on STN: 7 Aug 1990

AB Freeze-resistant overwintering larvae of the stag beetle Ceruchus piceus do not produce antifreezes in winter, but instead lower their supercooling points by seasonal removal of lipoprotein ice nucleators (LPINs) from the hemolymph. The normal lipid transport function of these lipoprotions becomes less essential during winter because of the low temperatures and the diapause state of the larvae. Adipokinetic hormone (AKH) and juvenile hormone (JH) were shown to be involved in the control of supercooling abilities and **LPIN** levels. Treatment of midwinter larve with AKH resulted in an increase in ice nucleator activity within 2 h, associated with elevated levels of LPINs, as demonstrated by Western blots derived from native PAGE gels **probe** with polyclonal antibodies to the LPINs. AKH also stimulated the release of **LPIN** in vitro from cultured fat bodies. In contrast, JH treatments of larvae with high hemolymph ice nucleator contents (either autumn or spring larvae) caused a decrease in ice nucleator activity and supercooling points. However, Western blots showed increased **LPIN** levels in these JH treated larvae. Apparently, this JH-induced, inactive form of **LPIN** lacks some component(s) essential for ice nucleator activity.

L15 ANSWER 3 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:311756 BIOSIS
DOCUMENT NUMBER: PREV198478048236; BA78:48236
TITLE: PHENYLALANYL AND TYROSYL SIDE CHAIN MOBILITY IN THE PHAGE M-13 COAT PROTEIN RECONSTITUTED IN PHOSPHO LIPID VESICLES.
AUTHOR(S): DETTMAN H D [Reprint author]; WEINER J H; SYKES B D
CORPORATE SOURCE: DEP BIOCHEM, UNIV ALBERTA, EDMONTON, ALBERTA T6G 2H7, CANADA
SOURCE: Biochemistry, (1984) Vol. 23, No. 4, pp. 705-712.
CODEN: BICHAW. ISSN: 0006-2960.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Analyses of the internal motions of proteins have increased the knowledge of protein structure in relation to function. These analyses were done, primarily, for water-soluble proteins, whose amino acid residues may experience 2 types of environments: the aqueous solvent outside or the hydrophobic core inside the protein. Residues on membrane proteins may be influenced by yet a third type of environment, that provided by the surrounding lipids. Quantitation of the motions within membrane proteins is required to determine the extent to which this third environment contributes to membrane protein structure/activity. The behavior of the major coat protein of the filamentous coliphage, M13, was studied when reconstituted into vesicles consisting of 80% dimyristoylphosphatidylcholine, 10% cardiolipin and 10% dipalmitoylphosphatidic acid, by weight. The protein had been labeled, in vivo, with 3-fluoro analogs of phenylalanine and tyrosine, thus providing specific labels of the hydrophilic and hydrophobic regions of the protein, respectively, for study using 19F NMR. To determine the exposure and orientation of the vesicle-bound coat protein, chymotryptic digestion and temperature experiments were done. Chymotryptic digestion, monitored by 19F NMR and paper electrophoresis, showed that the protein was incorporated symmetrically, as both the N- and C-terminal F-Phe residues were susceptible to the protease. The F-Tyr residues though were protected by the lipid bilayer. Temperature studies, where an 8-fluoro

analog of dipalmitoylphosphatidylcholine (FDPPC) was included as a lipid **probe**, demonstrated that the motions of both the F-Tyr and 8-FDPPC were affected by the fluidity state of the lipid, while the F-Phe mobility was not. Thus, the F-Phe and F-Tyr labels are reporting from the aqueous and bilayer environments, respectively. Quantitation of the ring motions of the F-Phe and F-Tyr residues was done through computer simulation of the 19F NMR resonance line width, NOE (nuclear Overhauser effect), and T1 data, meausred at 303 K. The computer algorithm was based on a model allowing the residue rings to wobble about the .alpha..beta.-bond and rotate about the .beta..gamma.-bond; the overall vesicle tumbling was assumed to have spherical symmetry. Both the F-Phe and F-Tyr data were most closely simulated when the wobble frequency about the .beta..beta.-bond was 2 .times. 108 s-1 and the rotation frequency about the .beta..gamma.-bond was 4 .times. 108 s-1. Both residues also seem to interact with neighboring molecules: the F-Tyr with passing lipids while the F-Phe with either phospholipid head groups or other amino acids. The difference between the 2 residues was in the angle through which the rings wobbled: The F-Tyr ring wobble angle was .+-. 75.degree. while the F-Phe angle was .+-. 90.degree.. As well, there is greater backbone motion for the hydrophilic ends containing the F-Phe residues relative to the transmembranal region, where the F-Tyr residues are found. Although the hydrohilic termini are allowed larger amplitudes of motion compared to the region of the protein surrounded with lipids, they are not freely moving about in solution but are either themselves structured or otherwise being restricted at the membrane surface. In turn, the motions found for the F-Tyr residues are comparable to those of a tyrosine buried in a hydrophobic pocket of a water-soluble protein. This indicates that surrounding a residue with lipids in the liquid-crystalline state is not more restrictive than surrounding a residue with other amino acid side chains.

L15 ANSWER 4 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:283580 BIOSIS
DOCUMENT NUMBER: PREV198478020060; BA78:20060
TITLE: THERMAL ADAPTATION OF TETRAHYMENA MEMBRANES WITH SPECIAL REFERENCE TO MITOCHONDRIA 2. PREFERENTIAL INTERACTION OF CARDIO **LIPIN** WITH SPECIFIC MOLECULAR SPECIES OF PHOSPHO LIPID.
AUTHOR(S): OHKI K [Reprint author]; GOTO M; NOZAWA Y
CORPORATE SOURCE: DEP BIOCHEM, GIFU UNIV SCH MED, 40, TSUKASAMACHI, GIFU 500, JPN
SOURCE: Biochimica et Biophysica Acta, (1984) Vol. 769, No. 3, pp. 563-570.
CODEN: BBACAQ. ISSN: 0006-3002.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB A specific effect of cardiolipin on fluidity of mitochondrial membranes was demonstrated in Tetrahymena cells acclimated to a lower temperature in a previous report. This was further confirmed by the experiment using fluorescence polarization of 1,6-diphenyl-1,3,5-hexatriene (DPH). Anisotropy of DPH for microsomal and pellicular total lipids from Tetrahymena cells showed that membrane fluidity of these lipids increased gradually as the cells were incubated at 15.degree. C after the shift down of growth temperature from 39.degree. C. Membrane fluidity of mitochondrial total lipids was kept constant up to 10 h. This finding is compatible with the result obtained using spin **probe** in the previous report. The break-point temperature of DPH anisotropy was not changed in mitochondrial lipids; those temperatures in pellicular and microsomal lipids lowered during the incubation of 15.degree. C. Interaction between cardiolipins and various phospholipids, which were isolated from Tetrahymena cells grown at 39.degree. or 15.degree. C and synthesized chemically, was investigated extensively using a spin labeling technique. The addition of cardiolipins from Tetrahymena cells grown at

either 39.degree. or 15.degree. C did not change the membrane fluidity (measured at 15.degree. C) of phosphatidylcholine from whole cells grown at 39.degree. C. Both cardiolipins of 39.degree. C-grown and 15.degree. C-grown cells decreased the membrane fluidity of phosphatidylcholine from Tetrahymena cells grown at 15.degree. C. The same results were obtained for phosphatidylcholines of mitochondria and microsomes. Membrane fluidity of phosphatidylethanolamine, isolated from cells grown at 15.degree. C, was reduced to a small extent by Tetrahymena cardiolipin; 39.degree. C-grown cells was not changed. Representative molecular species of phosphatidylcholines of cells grown at 39.degree. and 15.degree. C were synthesized chemically; 1-palmitoyl-2-oleoylphosphatidylcholine for 39.degree. C-grown cells and dipalmitoleoylphosphatidylcholine for 15.degree. C-grown ones. By the addition of Tetrahymena cardiolipin, the membrane fluidity of 1-palmitoyl-2-oleoylphosphatidylcholine was not changed but that of dipalmitoleoylphosphatidylcholine was decreased markedly. These phenomena were caused by Tetrahymena cardiolipin. Bovine heart cardiolipin, which has a different composition of fatty acyl chains from the Tetrahymena one, exerted only a small effect.

L15 ANSWER 5 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:352535 BIOSIS
DOCUMENT NUMBER: PREV198478089015; BA78:89015
TITLE: CHARACTERIZATION OF CALCIPHORIN BY LASER EXCITED EUROPIUM LUMINESCENCE.
AUTHOR(S): HERRMANN T R [Reprint author]; JAYAWEERA A R; AMBUDKAR I S; SHAMOO A E
CORPORATE SOURCE: MEMBRANE BIOCHEMISTRY RES LAB, DEP BIOLOGICAL CHEMISTRY, UNIV MD, SCH MED, 660 WEST REDWOOD ST, BALTIMORE, MD 21201, USA
SOURCE: Biochimica et Biophysica Acta, (1984) Vol. 774, No. 1, pp. 11-18.
CODEN: BBACAQ. ISSN: 0006-3002.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB There is some question whether the Ca binding characteristics of calciphorin are due to contaminating phospholipids. To differentiate protein ion binding from ion binding by phospholipids or contaminating detergent, the use of Eu(III) as a metal-binding-site **probe** is described, and the interaction of Eu(III) with calciphorin, cardiolipin, deoxycholate and digitonin is characterized. The luminescence excitation pattern of Eu(III) bound to the calciphorin preparation clearly differentiates it from Eu(III) interactions with the possible contaminants. In addition, the effect of the luminescence decay constant of Eu(III) bound to calciphorin on the mole fraction of H2O in a mixture of H2O/2H2O indicates that all except .apprx. 0.8 of the 9 to 10 water molecules coordinating Eu(III) in solution are stripped off upon binding to calciphorin. This also contrasts with the data for the possible contaminants.

L15 ANSWER 6 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1983:212949 BIOSIS
DOCUMENT NUMBER: PREV198375062949; BA75:62949
TITLE: AGING DEPENDENT MODIFICATION OF LIPID COMPOSITION AND LIPID STRUCTURAL ORDER PARAMETER OF HEPATIC MITOCHONDRIA.
AUTHOR(S): VORBECK M L [Reprint author]; MARTIN A P; LONG J W JR; SMITH J M; ORR R R JR
CORPORATE SOURCE: DEP OF PATHOL, UNIV OF MO-COLUMBIA, SCH OF MED, COLUMBIA, MO 65212, USA
SOURCE: Archives of Biochemistry and Biophysics, (1982) Vol. 217, No. 1, pp. 351-361.
CODEN: ABBIA4. ISSN: 0003-9861.
DOCUMENT TYPE: Article

FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB The effect of aging on the lipid composition of hepatic mitochondria was determined using a rigorously defined group of Fischer 344 rats with known survivorship data. The age groups studied included mature adults as controls (8.5 mo., 100% survivorship); an intermediate aged group (17.5-mo., 90% survivorship); and an aged group (29 mo., 20% survivorship). Lipid extracts of mitochondria were prepared using chloroform-methanol (2:1, by volume) and total phospholipid-Pi cholesterol (free and esterified), and phospholipid composition were determined. In the aged animals, total phospholipid-Pi decreased significantly (P = 0.019) whereas cholesterol increased (P = 0.048) with a progressive aging-dependent increase in the molar ratio of cholesterol/phospholipid. The lower total phospholipid content of hepatic mitochondria from the aged 29 mo. animals was due primarily to decreases in the major phospholipids with the most notable decrease being in cardiolipin (.apprx. 39%). Steady-state fluorescence polarization using 1,6-diphenyl-1,3,5-hexatriene as the **probe** was used to estimate the lipid structural order parameter of hepatic mitochondria. There was a highly significant (P = 0.01) aging-dependent increase in the lipid structural order parameter which correlated well with the increased molar ratio of cholesterol/phospholipid in the hepatic mitochondria isolated from the aged animals. The data suggest alterations in mitochondria membrane lipid-protein interactions in aging and are consistent with the hypothesis of impairment of membrane function in the aging process.

L15 ANSWER 7 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1981:278485 BIOSIS
DOCUMENT NUMBER: PREV198172063469; BA72:63469
TITLE: MEMBRANES AND PHOSPHO LIPIDS OF LIVER MITOCHONDRIA FROM CHRONIC ALCOHOLIC RATS ARE RESISTANT TO MEMBRANE DISORDERING BY ALCOHOL.
AUTHOR(S): WARING A J [Reprint author]; ROTTENBERG H; OHNISHI T; RUBIN E
CORPORATE SOURCE: DEP PATHOL AND LAB MED, HAHNEMANN MED COLL, PHILADELPHIA, PENNSYLVANIA 19102, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1981) Vol. 78, No. 4, pp. 2582-2586.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Using the spin **probe** 5-doxylstearic acid, the structural perturbations of rat liver mitochondrial membranes produced by exposure to ethanol in vitro and by chronic ethanol feeding were studied. The addition of ethanol in vitro to mitochondria from control animals fluidized the membranes, as evidenced by a pronounced decrease in the order parameter. In membranes from rats fed ethanol chronically, there was no effect on the order parameter. This resistance of the mitochondrial membranes from chronically intoxicated animals to the fluidizing effect of ethanol resulted from a change in the composition of the phospholipids, because the same differential response to ethanol was observed in vesicles of mitochondrial phospholipids extracted from control and chronically treated rats. In the presence of 0.025-0.1 M ethanol, a range that prevailed in the blood of chronic alcoholics, the order parameter of mitochondrial membranes from rats fed ethanol was comparable to that of control membranes without ethanol in vitro. Analysis of extracted mitochondrial phospholipids showed that the cardiolipin from ethanol-fed animals had fatty acyl residues that were more saturated than those of controls. Mitochondria from chronic alcoholic rats were more resistant to uncoupling by ethanol at physiological temperature. An adaptive change in the phospholipid composition evidently led to structural alterations, which resulted in increased resistance to

disruption of mitochondrial membranes by ethanol. These changes in lipid composition and structure may explain many of the mitochondrial abnormalities reported to result from chronic ethanol intoxication.

L15 ANSWER 8 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1982:201724 BIOSIS
DOCUMENT NUMBER: PREV198273061708; BA73:61708
TITLE: THERMAL ADAPTATION OF TETRAHYMENA-PYRIFORMIS MEMBRANES WITH SPECIAL REFERENCE TO MITOCHONDRIA ROLE OF CARDIO **LIPIN** IN FLUIDITY OF MITOCHONDRIAL MEMBRANES.
AUTHOR(S): YAMAUCHI T [Reprint author]; OHKI K; MARUYAMA H; NOZAWA Y
CORPORATE SOURCE: DEP BIOCHEM, GIFU UNIV SCH MED, TSUKASAMCHI-40, GIFU
SOURCE: Biochimica et Biophysica Acta, (1981) Vol. 649, No. 2, pp. 385-392.
CODEN: BBACAQ. ISSN: 0006-3002.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB During temperature acclimation of T. pyriformis, the changes in fluidity and composition of total lipids from 3 membrane fractions, mitochondria pellicles and microsomes were studied by a spin-label technique using a stearate **probe** and TLC and GLC. The increase of fluidity observed in microsomal and pellicular lipids following the temperature shift from 39-15.degree. C corresponds with the increase of the ratio of total unsaturated to saturated fatty acid content. Despite the increase of this ratio, the fluidity of mitochondrial lipids was constant up to 10 h after the temperature shift. The fluidity of total lipids of mitochondria isolated from Tetrahymena cells grown at 39.degree. C was unchanged by removal of cardiolipin; cardiolipin-depleted lipids of mitochondria from 15.degree. C-acclimated cells showed a decrease in fluidity. The re-addition of cardiolipin to the mitochondrial lipids depleted of cardiolipin restored the fluidity to the initial level, confirming the rigidifying effect of cardiolipin in cold-acclimated cells. Cardiolipin may be implicated in maintaining consistent fluidity of mitochondrial membranes against change in thermal environment.

L15 ANSWER 9 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1981:205062 BIOSIS
DOCUMENT NUMBER: PREV198171075054; BA71:75054
TITLE: EVIDENCE OF A COMPLEX BETWEEN ADRIAMYCIN DERIVATIVES AND CARDIO **LIPIN** POSSIBLE ROLE IN CARDIO TOXICITY.
AUTHOR(S): GOORMAGHTIGH E [Reprint author]; RUYSSCHAERT J M; CHATELAIN P; CASPERS J
CORPORATE SOURCE: LAB CHIM, PHYS MACROMOL AUX INTERFACES, UNIV LIBRE DE BRUXELLES, CP 206/2, BLVD DU TRIOMPHE, 1050 BRUXELLES, BELG
SOURCE: Biochemical Pharmacology, (1980) Vol. 29, No. 21, pp. 3003-3010.
CODEN: BCPCA6. ISSN: 0006-2952.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Most of the mitochondrial damage induced by antimitotic [and antineoplastic] drugs of the adriamycin family could be due to the high affinity of these drugs for the membrane [in vertebrates]. The prime interaction between the anthracycline drug and this membrane would explain specific alterations observed on mitochondria. Cardiolipin has been proposed as a privileged target. This hypothesis was tested. Model membranes (lipid monolayers, liposomes) were used to demonstrate the interaction between these anthracycline drugs and different phospholipids. A new surface potential technique showed the specificity of adriamycin derivatives for cardiolipin; no complexation was observed with neutral phospholipids (dipalmitoyl lecithin and egg lecithin). Association constants were evaluated, a good correlation was obtained between the mitochondrial toxicity of each drug and its affinity for cardiolipin.

Fluorescence measurements were carried out to locate precisely the position of the drug in the lipid bilayer. Perturbations of the lipid organization after complex formation were analyzed using phospholipase A2 as an enzymic **probe**.

L15 ANSWER 10 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1980:239504 BIOSIS
DOCUMENT NUMBER: PREV198070032000; BA70:32000
TITLE: VARIABLE INTERACTION OF SPIN LABELED HUMAN MYELIN BASIC PROTEIN WITH DIFFERENT ACIDIC LIPIDS.
AUTHOR(S): STOLLERY J G [Reprint author]; BOGGS J M; MOSCARELLO M A
CORPORATE SOURCE: DEP BIOCHEM, HOSP SICK CHILD, TORONTO, ONT M5G 1X8 CAN
SOURCE: Biochemistry, (1980) Vol. 19, No. 6, pp. 1219-1226.
CODEN: BICHAW. ISSN: 0006-2960.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Myelin basic protein from the human CNS was covalently spin-labeled with an iodoacetamide spin-label at its 2 methionyl residues at positions 21 and 167 from the N terminus of the protein. The spin-labeled protein, which is thought to bind electrostatically to acidic lipids followed by interaction of some hydrophobic segments with the lipid bilayer, was added to lipid vesicles in order to monitor the behavior of the protein in the lipid environment. A variety of lipids were used with which the degree of hydrophobic interaction seems to vary. Due to the effect of the protein on the organization of these lipids, the hydrophobic interaction seems to be greatest for phosphatidylglycerol and phosphatidic acid and decreases in the order phosphatidylserine > cerebroside sulfate .gtoreq. phosphatidylethanolamine. The ESR spectra of the spin-labeled protein in lipid vesicles of phosphatidylglycerol and phosphatidic acid possessed 2 or 3 components at low temperatures, 1 immobilized and other more mobile components. At higher temperatures in these 2 lipids and in the other lipids at all temperatures, a single component mobile spectrum was observed with hyperfine splitting indicative of a relatively polar environment. The motional parameter .lambda.0 of the protein spin-label in vesicles was greater than that for the protein in solution and varied depending on the lipid. The greatest reduction of motion was observed with phosphatidylglycerol, followed in order by phosphatidic acid, cerebroside sulfate, phosphatidylserine, cardiolipin and phosphatidylethanolamine. Measurement of the protein spin-label mobility at temperatures where the lipids possessed identical order parameters (S = 0.4) suggested that the order of the hydrocarbon chains of the different lipids was not the main factor in determining the **probe** motion. The motion of the spin-label on the methionyl residues reflects different degrees of hydrophobic interaction of some regions of the protein with the bilayer and attribute this variability in hydrophobic interaction to the occurrence of intermolecular eletrostatic and H- bonding for some of the lipids.

L15 ANSWER 11 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1981:49810 BIOSIS
DOCUMENT NUMBER: PREV198120049810; BR20:49810
TITLE: DIFFERENTIAL EFFECTS OF 2 CYTIDINE ANALOGS IN **NUCLEIC-ACID** PHOSPHO LIPID SYNTHESIS IN P-388 LEUKEMIC CELLS.
AUTHOR(S): JELSEMA C L [Reprint author]; MERRITT W D
CORPORATE SOURCE: MIDWEST CHILD CANCER CENT, MED COLL WIS, MILWAUKEE, WIS 53233, USA
SOURCE: European Journal of Cell Biology, (1980) Vol. 22, No. 1, pp. 506.
Meeting Info.: 2ND INTERNATIONAL CONGRESS ON CELL BIOLOGY, BERLIN, WEST GERMANY, AUG. 31-SEPT. 5, 1980. EUR J CELL BIOL.
CODEN: EJCBDN. ISSN: 0171-9335.

DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH

L15 ANSWER 12 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1981:167885 BIOSIS
DOCUMENT NUMBER: PREV198171037877; BA71:37877
TITLE: IDENTIFICATION OF THE SUBUNITS OF BOVINE HEART MITOCHONDRIAL NADH DEHYDROGENASE THAT ARE EXPOSED TO THE PHOSPHO LIPID BI LAYER BY PHOTO LABELING WITH 5 IODONAPHTH-1-YL AZIDE.
AUTHOR(S): EARLEY F G P [Reprint author]; RAGAN C I
CORPORATE SOURCE: DEP BIOCHEM, UNIV SOUTHAMPTON, SOUTHAMPTON SO9 3TU, ENGL, UK
SOURCE: Biochemical Journal, (1980) Vol. 191, No. 2, pp. 429-436. ISSN: 0264-6021.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Mitochondrial NADH dehydrogenase may be isolated from bovine heart as a lipoprotein complex (Complex I or NADH-ubiquinone oxidoreductase). Polypeptide subunits exposed to the hydrophobic region of the phospholipid bilayer were identified by photolabeling with the hydrophobic **probe**, 5-[125I]iodonaphth-1-yl azide. Chaotropic resolution of the labeled enzyme showed that the hydrophilic flavoprotein and Fe-protein fragments of the enzyme were not in contact with the phospholipid bilayer. When Complex I that had been partially depleted of phospholipids was photolabeled, incorporation of radioactivity into certain polypeptides was increased, indicating either conformational changes in the protein or preferential association of these polypeptides with residual cardiolipin. A model of NADH dehydrogenase structure is proposed on the basis of these results and those obtained with hydrophilic probes by Smith and Ragan.

L15 ANSWER 13 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1977:184298 BIOSIS
DOCUMENT NUMBER: PREV197764006662; BA64:6662
TITLE: CHANGES IN THE PHOSPHO LIPID BI LAYER STRUCTURE DURING THE ADSORPTION OF FERRI CYTOCHROME C ON ITS SURFACE.
AUTHOR(S): OBRAZTSOV V V; KOBELEV V S; TENCHOV B I; SELISHCHEVA A A; SIBEL'DINA L A; KOZLOV YU P; KAYUSHIN L P
SOURCE: Biokhimiya, (1976) Vol. 41, No. 11, pp. 2015-2020. CODEN: BIOHAO. ISSN: 0320-9725.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable
AB Changes in the mobility of phospholipid molecules in liposome membranes during adsorption of ferricytochrome c were studied by NMR and EPR spectroscopy. The interaction of the cytochrome molecule with the liposomes causes the broadening of 1H-NMR signals of hydrophobic as well as polar groups in cardiolipin and phosphatidylcholine in the presence of lauric or phosphatidic acid. This broadening of 1H-NMR signals in hydrophobic groups may be caused by a decrease in the rate of lateral diffusion of phospholipid molecules. Changes in the correlation time of hydrophobic spin-**probe** in liposomes containing phosphatidylcholine and cardiolipin with an increase of ferricytochrome c concentration were also observed. These changes suggest that the formation of protein-phospholipid clusters impairs the regular structure of the phospholipid bilayer.

L15 ANSWER 14 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1975:178621 BIOSIS
DOCUMENT NUMBER: PREV197560008617; BA60:8617
TITLE: ESR STUDIES ON THE LIPID PROTEIN INTERACTION BETWEEN CARDIO **LIPIN** AND ANTI CARDIO **LIPIN** ANTIBODIES.

AUTHOR(S): SCHIEFER H-G; SCHUMMER U; HEGNER D; GERHARDT U; SCHNEPEL G H
SOURCE: Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie, (1975) Vol. 356, No. 3, pp. 293-300.
CODEN: HSZPAZ. ISSN: 0018-4888.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable

L15 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1926:20557 CAPLUS
DOCUMENT NUMBER: 20:20557
ORIGINAL REFERENCE NO.: 20:2516b-f
TITLE: Studies on bios. I
AUTHOR(S): Suzuki, Bunsuke; Taira, Tomosune
SOURCE: Nippon Kagaku Kaishi (1921-47) (1925), 45, 299-311
CODEN: NIKWAB; ISSN: 0369-4208
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Bios was prepd. by 3 methods: (1) Com. orizanin was extd. with H2O and treated with an excess Al2(SO4)2. The yellow Al ppt. was suspended in H2O, treated with dil. H2SO4 and again with Al2(SO4)3. The final filtrate was concd. at a low temp. and extd. with alc. The alc. ext. was concd., and treated with H2O. On removal of alc. from the residue, a dark brown ppt. formed which contained crude bios. (2) The aq. ext. of orizanin was treated with a large amt. of acetone, and satd. with (NH4)2SO4. The acetone layer, contg. bios, was then treated as in method (1). (3) By far a greater amt. of bios was obtained from certain waste products of com. orizanin manuf. When the alc. ext. of fat-free rice bran was freed from alc. and its aq. soln. let stand, a muddy ppt. was produced, which contained **lipin**-like substances, **nucleic acid**
, etc. These waste products which were thrown away in the manuf. of orizanin, when extd. with a mixt. of alc.-Et2O and then again with Et2O, gave a yellow residue which contained a satisfactory amt. of crude bios. The dried crude bios is insol. in H2O and ordinary solvents (except in pyridine); MeOH dissolved it to the extent of 1.5%. The bios can be freed from **nucleic acid** by means of MeOH, and further
purified by passing CO2 into an alk. soln. of the product. The final product had the const. compn. of C62H81NO27. It forms salts with org. and inorg. bases, dissolves in alkali, but is pptd. by acids. Its alk. soln. diffuses through a colloidal membrane. It is incompletely pptd. by phosphotungstic, phosphomolybdic and tannic acids, basic lead acetate and HgCl2 solns. Pptg. solns. having oxidizing powers are apt to be reduced by it. Folin's uric acid reagent is turned greenish blue; Fehling and ammoniacal AgNO3 solns. also are reduced. It shows tannin reactions, pptg. gelatin and other reagents. When bios is boiled with 1.5% HCl for 1.5 hrs., a beautiful cryst. compd. is produced which has the compn. C10H8NO4, identical with Suzuki's .beta.-acid. The filtrate contains a hexose (the osazone m. 208, identical with glucosazone). Pure bios when nitrated gives picric acid (m. 122.degree.). The nitration of .beta.-acid does not give picric acid, but another nitro compd. The results of biological expts. with various fractions of the pptn. of pure bios are given in 4 tables and 3 curves. The pure bios thus prepd. corresponds to that of Wildiers, with the exception that it does not dissolve in H2O. It has no antipolyneuritic power, but very strongly promotes the growth of yeast. It consists of glucose, .beta.-acid and a substance which goes over to picric acid on nitration. Since .beta.-acid seems to constitute the nucleus of the bios, S. and T. suggest another name for it, biogenic acid.

=> d his

(FILE 'HOME' ENTERED AT 13:39:34 ON 30 JAN 2004)

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 13:39:56 ON 30 JAN 2004

L1 384 S REUE K?/AU OR PETERFY M?/AU
L2 14 S L1 AND (LPIN OR LIPIN)
L3 8 DUP REM L2 (6 DUPLICATES REMOVED)
L4 1086 S (LIPIN OR LPIN)
L5 9 S L4 AND (GENE EXPRESSION)
L6 7 DUP REM L5 (2 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 13:45:52 ON 30 JAN 2004

FILE 'MEDLINE, BIOTECHDS, EMBASE, BIOSIS, SCISEARCH, CANCERLIT, CAPLUS'
ENTERED AT 13:47:49 ON 30 JAN 2004

L7 16 S L4 AND ADIPOSE
L8 10 DUP REM L7 (6 DUPLICATES REMOVED)
L9 9 S L4 AND MRNA
L10 4 DUP REM L9 (5 DUPLICATES REMOVED)
L11 17 S L4 AND SCREEN?
L12 16 DUP REM L11 (1 DUPLICATE REMOVED)
L13 1045 DUP REM L4 (41 DUPLICATES REMOVED)
L14 15 S L13 AND (NUCLEIC ACID OR PROBE OR GENE PRODUCT)
L15 15 DUP REM L14 (0 DUPLICATES REMOVED)

OURNAL OF BIOLOGICAL CHEMISTRY, (1989 May 15) 264 (14)
7994-8003.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19890630

AB An autosomal recessive mutation, termed **fatty liver dystrophy** (fld), can be identified in neonatal mice by their enlarged and fatty liver (Sweet, H. O., Birkenmeier, E. H., and Davisson, M. T. (1988) Mouse News Letter 81, 69). We have examined the underlying metabolic abnormalities in fld/fld mice from postnatal days 3-40. Serum and hepatic triglyceride levels were elevated 5-fold in suckling fld/fld mice compared to their +/? littermates but abruptly resolved at the suckling/weaning transition. Blot hybridization analysis of liver and intestinal RNAs revealed a liver-specific increase in apolipoprotein (apo) A-IV and C-II **mRNA** concentrations (100- and 6-fold, respectively) that was limited to the suckling and early weaning stages in fld/fld mice. Resolution of these differences during the weaning period could not be delayed by prolonging suckling to the 20th postnatal day nor could the mutant phenotype be elicited in young adult animals with a high fat diet. Lipoprotein lipase (LPL) activity was reduced 16-fold in the white adipose tissue of fld/fld mice until the onset of weaning. Heart activity was decreased less than 2-fold, but there were no deficits in brown adipose tissue or liver. Hepatic lipase (HL) **mRNA** levels and activity were significantly reduced in fld/fld livers and sera, respectively, during the suckling period. Mapping studies show the fld locus to be distinct from loci encoding LPL, HL, and apoA-IV, and those responsible for the combined lipase deficiencies in cld/cld and W/Wv mice. These data suggest that the fld mutation is associated with developmentally programmed tissue-specific defects in the neonatal expression of LPL and HL activities and provide evidence for a new regulatory locus which affects these lipase activities. This mutation could serve as a useful model for (i) analyzing the homeostatic mechanisms controlling lipid metabolism in newborn mice and (ii) understanding and treating certain inborn errors in human triglyceride metabolism.

Altered gene expression pattern in the **fatty liver dystrophy** mouse reveals impaired insulin-mediated cytoskeleton dynamics.

AUTHOR: Klingenspor M; Xu P; Cohen R D; Welch C; Reue K

CORPORATE SOURCE: Department of Medicine, University of California, and The Lipid Research Laboratory, West Los Angeles Veterans Affairs Medical Center, Los Angeles, California 90073, USA.

CONTRACT NUMBER: HL28481 (NHLBI)

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Aug 13) 274 (33) 23078-84.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-AF054279; GENBANK-AF054280; GENBANK-AF054281; GENBANK-AF054282; GENBANK-AF054283

ENTRY MONTH: 199909

ENTRY DATE: Entered STN: 19990913
Last Updated on STN: 19990913
Entered Medline: 19990901

AB The mouse **fatty liver dystrophy** (fld) mutation is characterized by transient hypertriglyceridemia and fatty liver during the neonatal period, followed by development of a peripheral neuropathy. To uncover the metabolic pathway that is disrupted by the fld mutation, we analyzed the altered pattern of gene expression in the fatty liver of fld neonates by representational difference analysis of cDNA. Differentially expressed genes detected include a novel member of the Ras superfamily of small GTP-binding proteins, a novel Ser/Thr kinase, and several actin cytoskeleton-associated proteins including actin, profilin, alpha-actinin, and myosin light chain. Because these proteins have a potential functional link in the propagation of hormone signals, we investigated cytoskeleton dynamics in fld cells in response to hormone treatment. These studies revealed that preadipocytes from fld mice exhibit impaired formation of actin membrane ruffles in response to insulin treatment. These findings suggest that the altered **mRNA** expression levels detected in fld tissue represent a compensatory response for the nonfunctional fld gene and that the fld **gene product** may be required for development of normal insulin response.

L18 ANSWER 3 OF 5 MEDLINE on STN

ACCESSION NUMBER: 91268073 MEDLINE

DOCUMENT NUMBER: 91268073 PubMed ID: 2050689

TITLE: Characterization of the peripheral neuropathy in neonatal and adult mice that are homozygous for the **fatty liver dystrophy** (fld) mutation.

AUTHOR: Langner C A; Birkenmeier E H; Roth K A; Bronson R T; Gordon J I

CORPORATE SOURCE: Department of Biochemistry and Molecular Biophysics, Washington University School of Medicine, St. Louis, Missouri 63110.

CONTRACT NUMBER: CA34196 (NCI)
DK37960 (NIDDK)

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Jun 25) 266 (18) 11955-64.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199107

ENTRY DATE: Entered STN: 19910811
Last Updated on STN: 19910811

Entered Medline: 19910724

AB In a previous report (Langner, C. A., Birkenmeier, E. H., Ben-Zeev, O., Schotz, M. C., Sweet, H. O., Davisson, M. T., and Gordon, J. I. (1989) J. Biol. Chem. 264, 7994-8003), we characterized the early developmental phenotype of mice that were homozygous for the autosomal recessive **fatty liver dystrophy** (fld) mutation. Shortly after birth, these mice can be distinguished from their +/? littermates by large pale livers, hypertriglyceridemia, elevations in hepatic apolipoprotein A-IV and apoC-II **mRNA** levels, and tissue-specific decreases in lipoprotein lipase and hepatic lipase activities. These traits resolve by the early weaning period. We have now characterized a second feature of this mutation: a peripheral neuropathy that becomes manifest by an abnormal gait at the end of the second postnatal week and persists through adulthood. Electron microscopic studies of sciatic nerves from 4-day-to 1-year-old fld/fld mice demonstrated a variety of abnormalities including thin, poorly compacted myelin sheaths, active myelin breakdown, and enlarged Schwann cell mitochondria and nuclei. Western blot analysis of sciatic nerve homogenates prepared from 1 to 3-month-old fld/fld mice and their +/? littermates indicated that homozygous animals have striking reductions in two peripheral nerve myelin-associated proteins, P0 and P2. The steady-state level of apoE, a protein induced during nerve regeneration, is markedly elevated. Furthermore, two axon-specific proteins, neurofilament 68K and growth-associated 43 protein, display altered expression in adult fld/fld sciatic nerves. High performance thin-layer chromatography revealed deficiencies in phospholipids, glycosphingolipids, and some neutral lipids in fld/fld sciatic nerves harvested during the first several months of life (compared to their +/? littermates). Cholesterol esters were elevated in homozygotes. By contrast, no differences in brain lipids were noted between fld/fld animals and their +/? littermates. These data suggest that the fld mutation is associated with an abnormality of myelin formation (dysmyelination) as well as demyelination and axonal degeneration that persists despite apparent resolution of the neonatal hypertriglyceridemia and associated lipase abnormalities. These findings establish the fld/fld mouse as an excellent model system for analyzing homeostatic mechanisms that modulate lipid metabolism in newborn mice and for examining the pathogenesis of peripheral neuropathies associated with dyslipidemias.